

Systematic Review

Propolis as Natural Product in the Oral Cavity Bacterial Infections Treatment: A Systematic Review

Michał Otręba ^{1,*} , Łukasz Marek ² , Natalia Tyczyńska ¹, Jerzy Stojko ³ , Anna Kurek-Górecka ⁴ ,
Michał Górecki ¹ , Paweł Olczyk ⁴  and Anna Rzepecka-Stojko ¹ 

- ¹ Department of Drug Technology, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Jedności 8, 41-200 Sosnowiec, Poland
- ² Department of Instrumental Analysis, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Jedności 8, 41-200 Sosnowiec, Poland
- ³ Department of Toxicology and Bioanalysis, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Ostrogórska 30, 41-200 Sosnowiec, Poland
- ⁴ Department of Community Pharmacy, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Kasztanowa 3, 41-200 Sosnowiec, Poland
- * Correspondence: motreba@sum.edu.pl

Abstract: The up-to-date records show that approximately 10% of people worldwide suffer from periodontal diseases and about 50% of adults have some sort of moderate oral cavity disease. Therefore, oral cavity diseases represent the group of the most common chronic inflammatory diseases in the world. Thus, novel, natural, safe, and effective methods of treatment need to be found. In this study, a systematic search was performed in PubMed and Google Scholar up to March 2022 to select research evaluating the activity of propolis against bacteria responsible for oral cavity diseases. Peer-reviewed journals in English containing information about the *in vitro* and *in vivo* studies were included in our research. We excluded the records without access, written in another language than English, thesis or book chapters, and review papers, and we rejected the texts when the authors did not write about the antibacterial activity. Collected results of the inhibition zone as well as average MIC and MBC values indicated that propolis exhibits antimicrobial activity against the strains of bacteria which cause, e.g., periodontitis, gingivitis, caries, subgingival plaque, supragingival plaque, recurrent aphthous ulcers (RAS), and pharyngitis. However, before propolis can be commonly used, more research is needed to fully understand its composition and antibacterial mechanism of action.

Keywords: propolis; antimicrobial activity; oral cavity diseases; bacterial infections



Citation: Otręba, M.; Marek, L.; Tyczyńska, N.; Stojko, J.; Kurek-Górecka, A.; Górecki, M.; Olczyk, P.; Rzepecka-Stojko, A. Propolis as Natural Product in the Oral Cavity Bacterial Infections Treatment: A Systematic Review. *Appl. Sci.* **2022**, *12*, 10123. <https://doi.org/10.3390/app121910123>

Academic Editor: Bo Wang

Received: 5 September 2022

Accepted: 4 October 2022

Published: 9 October 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

People have been taking care of their teeth since ancient times, showing how important it is to maintain good oral health. Oral health is constantly evolving due to development in technology and medicine. Lately, attention has been paid to natural methods of treating oral cavity diseases due to their reduced side effects [1]. According to the ADAH (American Dental Hygienists' Association) in 2022, almost 80% of Americans will have at least one cavity before age of 17, nearly 80% of Americans have some level of gum disease and 40% of children under the age of 3 years have never been to the dentist [1]. On the other hand, in the United Kingdom (UK), regular visits to a dentist have not been confirmed by 39%, almost 66% of adults have visible plaque, caries has been diagnosed in 31% of adults, about 74% of adults have had a tooth extraction and over 3 million people in the UK suffer from oral pain [2]. In the UK, gingivitis and periodontitis caused by plaque constitute the most common oral conditions. Additionally, evidence from 9th November 2021 shows that around 10% of people worldwide suffer from periodontal diseases, and about 50% of adults have some sort of moderate oral disease. Thus, the mentioned diseases can belong to the group of most frequently diagnosed chronic inflammatory diseases in the world [3].

Table 1 depicts the main bacterial strains which are responsible for oral cavity microbial infections.

Table 1. Bacterial strains responsible for infections of the oral cavity.

Disease	Bacteria
Caries	<i>Actinomyces israelii</i> [4,5], <i>Actinomyces naeslundii</i> [6], <i>Actinomyces odontolyticus</i> [7], <i>Actinomyces viscosus</i> [6], <i>Alexandrium minutum</i> [8,9], <i>Bacteroides ovatus</i> [8,10], <i>Bifidobacterium longum</i> [4,11], <i>Bifidobacterium adolescentis</i> [4,11], <i>Clostridium ramosum</i> [4,12], <i>Clostridium perfringens</i> [4,12], <i>Eikenella corrodens</i> [7], <i>Fusobacterium nucleatum</i> [7], <i>Lactobacillus acidophilus</i> [7], <i>Lactobacillus casei</i> [13–15], <i>Lactobacillus fermentum</i> [8,10], <i>Peptoniphilus asaccharolyticus</i> [16,17], <i>Peptostreptococcus micros</i> [18,19], <i>Porphyromonas endodontalis</i> [6], <i>Porphyromonas gingivalis</i> [6], <i>Prevotella melaninogenica</i> [18,19], <i>Prevotella dentica</i> [6], <i>Staphylococcus aureus</i> [8,20], <i>Streptococcus cricetus</i> [21], <i>Streptococcus mitis</i> [7], <i>Streptococcus mutans</i> [21], <i>Streptococcus salivarius</i> [15], <i>Streptococcus sanguinis</i> [6], <i>Streptococcus sobrinus</i> [21], <i>Streptococcus viridans</i> [16,22]
Gingivitis	<i>Actinomyces israelii</i> [23], <i>Actinomyces naeslundii</i> [6,24], <i>Actinomyces viscosus</i> [6,24], <i>Campylobacter gracilis</i> [23], <i>Clostridium perfringens</i> [23]
Periodontitis	<i>Actinomyces israelii</i> [25], <i>Actinomyces naeslundii</i> [25], <i>Actinomyces odontolyticus</i> [7], <i>Aggregatibacter actinomycetemcomitans</i> [26], <i>Capnocytophaga ochracea</i> [8,25], <i>Eikenella corrodens</i> [7], <i>Fusobacterium nucleatum</i> [7,27], <i>Fusobacterium periodonticum</i> [25], <i>Fusobacterium varium</i> [16,28], <i>Lactobacillus spp.</i> [29], <i>Peptostreptococcus anaerobius</i> [19,30], <i>Porphyromonas gingivalis</i> [31,32], <i>Prevotella bivia</i> [16,33], <i>Prevotella intermedia</i> [27], <i>Prevotella nigrescens</i> [25], <i>Streptococcus bovis</i> [13,34], <i>Streptococcus gordonii</i> [35,36], <i>Streptococcus intermedius</i> [37], <i>Streptococcus intermermedius</i> [37], <i>Streptococcus mutans</i> [29], <i>Tannerella forsythia</i> [25,38], <i>Treponema denticola</i> [25,38], <i>Veillonella parvula</i> [19,39]
Pharyngitis	<i>Streptococcus pyogenes</i> [40]
Recurrent aphthous ulcers (RAS)	<i>Streptococcus sanguinis</i> [6]
Subgingival plaque	<i>Prevotella intermedia</i> [27], <i>Prevotella oralis</i> [19,41], <i>Porphyromonas gingivalis</i> [27,38], <i>Tannerella forsythia</i> [42]
Supragingival plaque	<i>Actinomyces naeslundii</i> [25,43], <i>Fusobacterium nucleatum</i> [43], <i>Neisseria subflava</i> [8,44], <i>Streptococcus mutans</i> [43], <i>Streptococcus oralis</i> [8,43], <i>Veillonella dispar</i> [43]

The medications which can be applied to treat or prevent diseases of the oral cavity, possible side effects of treatment, and the causes of tooth decay were described in our previous publication [45].

Propolis called “bee glue” is a gummy resinous material made by the honeybees (*Apis mellifera*) from resins they collect from leaf buds and bark of different plants [46]. The chemical content of propolis depends on the geographical zone of origin, specificity of local flora, plant sources, and the collection season [46,47]. Propolis is rich in biologically active compounds (over 300 compounds): resin and balsams (50–70%) [46], essential oils and wax (30–50%) [46], pollens (5–10%) [46], amino acids [46,47], enzymes (amber dehydrogenase, glucose-6-phosphatase, and acid phosphatases) [48], minerals (Mg, Ca, K, Na, Cu, Zn, Mn, Se, Fe, Si, Ni, Co, and V) [46,48,49], vitamins (A, B1, B2, B6, C, D, and E) [46–48], glucose [47], flavonoids (pinocembrin, acacetin, chrysin, rutin, luteolin, kaempferol, apigenin, myricetin, catechin, naringenin, galangin, caffeic and 3,4-dimethylcaffeic acids, isoferulic acid, tectochrysin, pinostrobin, and quercetin) [46,49–51], phenolic compounds (artepillin C) [46,50], aromatic acids (ferulic, cinnamic, caffeic, benzoic, butyric, salicylic, and *p*-cumaric) [47,49,50], esters (phenethyl ester) [48,50], terpenes (terpineol, camphor, geraniol, nerol, and farnesol) [48,49], and beta-steroids [48]. Bee glue possesses antioxidant activity (more potent than vitamin C), antibacterial, antiviral, antifungal, and anti-inflammatory properties [46].

The amount of 70 mg/day of propolis has been determined as a safe dose of propolis for a healthy person. More than 7.34 g/kg (LD₅₀) of propolis extract constitutes a median lethal dose for conscious mice, whereas 150 mg of pinocembrin (a component of propolis)

in a single dose can be considered safe. This confirms that propolis is a generally safe natural product [52]. The side effects of propolis that were observed are shown in Table 2.

Table 2. Side effects of propolis.

Type of Side Effect	Effect
More common adverse effect	Hypersensitivity (regard to topical application), resulting in allergic reactions (swelling, dermatitis, and urticarial) [52]
Specific (individual) cases	Severe swelling of the throat, anaphylactic shock after topical application [52]
Severe side effects (seldom occurs)	Laryngeal edema and anaphylactic shock [52]

Moreover, propolis therapy may also lead to stomatitis, contact dermatitis (only 1.2–6.6% of individuals [52]), cheilitis, and erythema multiforme [53].

This review aims to summarize up-to-date research on propolis as an effective substance for maintaining hygiene of the oral cavity and treatment of oral infections caused by bacteria. Therefore, we focused on the papers in which the researchers reported *in vitro* studies on bacterial strains which caused oral cavity infections and some *in vivo* studies which underlined the therapeutic potential of propolis.

2. Search Methodology

PubMed and Google Scholar were used in March 2022 to search for English-language papers containing phrases “(propolis) and (oral cavity) and (hygiene) and (antibacterial) or (antimicrobial)”. The analysis of the database led to selecting 1120 records from Google Scholar and 20,253 records from PubMed publications which could be related to the medical use of propolis (Figure 1). The search results were excluded when (1) there was no access, (2) another language than English was used, (3) they were thesis or book chapters, (4) review papers, and (5) there was no information about the antibacterial activity. The following were included into our study: (1) peer-reviewed journals in English in which there was the information about the (1) *in vitro* and (2) *in vivo* studies of various strains of bacteria responsible for oral cavity infections.

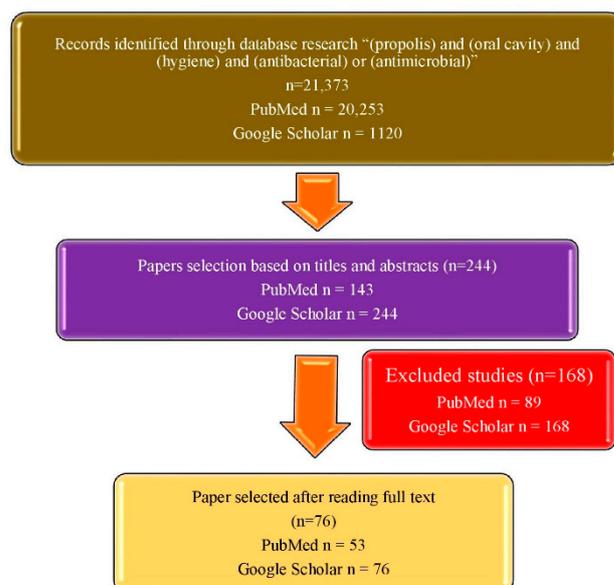


Figure 1. The process of selection of the papers.

3. Antibacterial Properties of Propolis: Mode of Action

Propolis interacts with lipids in the plasma membrane, increases membrane permeability, disrupts membrane potential and adenosine triphosphate (ATP) production, inhibits bacterial motility [49,53], cell envelope [54], efflux pumps [54], generates ion imbalance in the microenvironment of the bacteria [53], as well as inhibits bacterial proteins and nucleic acids synthesis [55].

Phenolic compounds and flavonoids play a crucial role in the antibacterial activity of propolis [47]. Flavonoids (pinocembrin and apigenin) have antibacterial activity against *S. mutans* and *S. sobrinus* [49]. Flavonoids (galangin, pinocembrin, and pinostrobin) increase bacterial membrane permeability, inhibit bacterial genetic coding, nucleic acid synthesis, the attachment and formation of biofilms, and energy metabolism of bacteria [52]. The B ring of flavonoids inhibits bacterial nucleic acid synthesis [55].

Up to now, three pathways leading to disruption of the bacterial membrane by propolis are known: (I) attaching to the bacteria cell wall, which leads to cell lysis and bacteria's death; (II) the interaction between the hydrophobic parts of the membrane and the polar headgroup of propolis; (III) ability to inhibit protein synthesis. Moreover, flavonoids are able to bind to bacterial cell walls leading to the lysis of the cells or inhibiting bacterial growth by the inhibition of topoisomerase IV-dependent deactivation activity [55]. Apigenin is a potent inhibitor of glucosyltransferases B and C [56], peptidoglycan synthesis, and β -lactamase enzymes, and it alters the outer and cytoplasmic membrane permeabilization [57]. Lipophilic properties of Tt-farnesol alter the permeability and fluidity of the cell membrane and affect its glycolytic activity, production–secretion of glucosyltransferases and acidurance [56]. Caffeic acid phenethyl ester also increases bacterial membrane permeability and inhibits bacterial RNA polymerase [58]. In case of *P. gingivalis*, artepillin C (a phenolic compound) causes membrane blebbing and is responsible for bacteriostatic activity [49]. 3-Prenyl-cinnamic acid allyl ester and 2-dimethyl-8-prenylchromene, which are found in propolis, also possess antimicrobial activity [49]. Propolis also inhibits the activity of glucosyltransferase enzyme via the synthesis induction of insoluble glycan. Thus, propolis possesses antimicrobial activity against *S. circuits*, *S. mutans*, and *S. sobrinus* [46].

The inhibition of the cell envelope synthesis is possible by the inhibition of (I) β hydroxyacyl-ACP dehydrase, (II) β -hydroxyacyl-acyl carrier protein dehydratase, (III) fatty acid synthase-type II (FAS-II) and (IV) Ala-Ala synthetase. Flavonoids are also able to inhibit the synthesis of cell envelopes. Quercetin, apigenin, and sakuranetin inhibit β hydroxyacyl-ACP dehydrase and act as competitive inhibitors of β -hydroxyacyl-acyl carrier protein dehydratase. β -hydroxyacyl-ACP is a key component for bacterial membrane and substrates for the acyltransferases (catalyze early steps in lipopolysaccharide biosynthesis), which are important for bacterial survival. Quercetin, kaempferol, fisetin, myricetin, and morin may inhibit FAS-II, which is important for membrane biogenesis. Apigenin, galangin, and kaempferol inhibit Ala-Ala synthetase [54].

Baicalein, morin, silibinin, sylimarin, 6-prenylapigenin, and isobavachalcon inhibit electron transport chain and ATP synthesis [54]. Galangin increases in potassium loss, leading to direct cytoplasmic membrane damage of the bacterial cell wall [57]. Cinnamic acid possesses antimicrobial activity, since it can inhibit the production and function of ATPases, cell division, and biofilm formation. This is possible due to damaging the bacterial cell membrane and disrupting the key metabolic pathways with a stress on the inhibition of intracellular pH homeostasis [49,55].

Quercetin, morin, luteolin, and rutin inhibit efflux pumps such as ATP-binding cassette (ABC) transporter, multi-antimicrobial and toxic compound extrusion (MATE) transporter, major facilitator MFS) transporter, small multidrug resistance (SMR) transporter, and resistance–nodulation cell division (RND) transporter, leading to the decreased level of inhibitory concentration [54].

The inhibition of protein synthesis is possible by the inhibition of RNA-polymerase, modulation of the crosstalk through the Toll-like receptor (TLR) of host–microbiota by flavonoids, and activating different chief protein kinases by flavonoids [55]. Apigenin,

catechin, quercetin, morin, and naringenin can cause cell membrane disruption and leakage of intracellular contents [54]. Flavonoids (flavanols, flavan-3-ols, and flavones) bind to topoisomerase II, resulting in cleavage of the DNA [54].

The inhibition of nucleic acid synthesis is possible by binding to (I) the bacterial DNA gyrase B subunit, (II) topoisomerase II as well as inhibition of (III) topoisomerase IV-dependent deactivation activity, (IV) dihydrofolate reductase (DHFR) and (V) helicase. Quercetin, ellagic acid, and apigenin bind to the bacterial DNA gyrase B subunit to inhibit ATPases activity and decrease bacterial activity [54,55]. Luteolin, morin, and myricetin inhibit helicase, while epigallocatechin-3-gallate (ECGC) inhibits dihydrofolate reductase (DHFR), which results in inhibiting the synthesis of nucleic acid and reducing the growth of bacteria [54].

Flavonoids may also inhibit bacterial motility because they “quickly arrest bacterial movement by blocking swarming motility to prevent bacterial adhesion as well as colonization because bacterial movement and attachment occur at different times” [54]. It is also believed that bee glue “wraps” around bacteria, leading to their elimination by the body’s immune system. The strong immune and inflammatory response may be stimulated by flavonoids, which are very potent inhibitors of eicosanoids production [46].

The anti-inflammatory mechanisms of propolis include the inhibition of cyclooxygenase (COX) and subsequent inhibiting biosynthesis of prostaglandins, and free radical scavenging. Additionally, nitric oxide synthesis is inhibited, the concentration of inflammatory cytokines is reduced, and immunosuppressive effects are observed [52]. Artepillin C possesses anti-inflammatory activity such as the modulation of NF- κ B and inhibition of prostaglandin E2 and nitric oxide [49]. Caffeic acid phenethyl ester inhibits the activity and expression of COX-2, while pinocembrin treatment of mice significantly reduces neuronal pro-inflammatory cytokines (TNF- α , IL-1, and IL-6), chemokines (intercellular adhesion molecule-1, vascular cell adhesion molecule-1), inducible nitric oxide synthase (iNOS), and aquaporin-4. Moreover, pinocembrin suppresses the nuclear translocation of NF- κ B and decreases TNF- α expression [52]. The summarized antimicrobial properties of propolis are presented in Figure 2.



Figure 2. The summarized antimicrobial activity of propolis.

4. Results

4.1. Selected Studies

A total of 244 records were selected for further analysis, and the inclusion was based on the titles and abstracts of papers published between 1991 and 2022. The selected papers were read, and 168 of them were considered inappropriate for our study. The researchers decided to include 76 original articles (2000–2022) into their systematic review, and the papers were classified into two groups, i.e., *in vitro* and *in vivo* studies (Figure 1).

4.2. Antibacterial Activity of Propolis in Oral Cavity Bacterial Infections

Propolis is useful in oro-dental care in treating aphthous and traumatic mouth ulcerations, and it also possesses a slightly anesthetic effect. The toothpaste containing propolis is useful for periodontal patients and hypersensitivity, while propolis liquid is used in the treatment of aphthous type oral ulcerations, denture trauma, and herpetic and nonspecific painful oral ulcerations. Mouthwash and gargling are used for the temporary relief of sore gums and throat [46]. In toothpaste and mouthwash, propolis acts as an anti-caulus agent [50]. Propolis mouthwash significantly reduces the bacterial count and plaque accumulation after 3 weeks of use, while propolis toothpaste reduces gingival inflammation [47]. The most useful is propolis tincture, since it “can be applied to areas where other preparations are not so effective in staying in place”, especially in the treatment of ulcers. During the treatment, a film of resin over the ulcer appears leading to pain relief and provides a healing barrier to further irritation [46].

4.2.1. In Vitro Studies

Koo et al. [6] examined how ethanolic extracts of propolis (EEP) from Brazil affected various strains of *Streptococcus spp.* The researchers used propolis from the following regions of the country: Northeastern Brazil (BA), Southeastern (MG), and Southern (RS) Brazil. It was observed that all EEPs had biological activity against *S. mutans*. On the other hand, the highest potency of EEP BA was recorded for all criteria of *in vitro* procedures that were assessed in this study. The latter suggested that EEP BA could constitute an effective anti-plaque/anti-caries agent. The antibacterial activity assays were carried out, and minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) of EEPs against *S. mutans*, *S. sobrinus*, and *S. cricetus* were determined. The values of MBC were four to eight times higher than the MIC values (Table 3). The authors observed also a marked inhibition of the adherence of *S. mutans* and *S. sobrinus* cells caused by EEPs, and the inhibition was significant at all concentrations when compared to the control (80% ethanol). Whereas, EEP BA in the concentration of 12.5 mg/mL inhibited cell adherence by 80% [6].

In the same year, Koo et al. [21] analyzed the impact of southeastern Brazilian propolis ethanolic extract (10%) against *S. sobrinus*, *S. sanguis*, *S. cricetus*, *S. mutans*, *A. naeslundii*, *A. viscosus*, *P. gingivalis*, *P. endodontalis*, and *P. denticola*. The researchers concluded that propolis could prevent dental caries and periodontal diseases. A significant increase in inhibition growth area after propolis extract treatment was observed for all bacterial strains. Moreover, in case of the control (80% ethanol), the zone of microbial growth was not observed. The biggest inhibition zone (about 9 mm) was observed for both *Actinomyces spp.* strains [21].

In 2003, Duarte et al. [59] analyzed how the crude ethanolic extract of propolis affected *S. mutans* and *S. sobrinus*. The researchers observed that propolis type 6 significantly inhibited the growth and adherence of *Streptococcus mutans*. It should be mentioned that there is a relationship between these biological activities and nonpolar components of propolis. The authors determined MIC, MBC, and how bacteria adhered to a glass surface. It is noteworthy that the antibacterial activity of the EEP, hexane, and chloroform fractions was recorded. The MICs and MBCs of the test compounds are presented in Table 3 [59].

Sawaya et al. [60] extracted Brazilian propolis from the São Paulo state using several solvents; therefore, they obtained extracts characterized by varied composition. The authors evaluated the activity of propolis against *S. pyogenes*, *S. mutans*, *S. salivarius*, and *S. sobrinus* with the use of *in vitro* assays. Moreover, serial dilution in tubes proved to be the most appropriate method to estimate the bactericidal activity of the propolis sample. It was observed that the synergistic effect of several components resulted in the bactericidal activity of propolis. These components were determined with the use of HPLC, and the most efficient extraction was recorded when 50% ethanol was the solvent. Serial dilution in tubes and agar plate diffusion were employed to assay the bacterial activity of the above-mentioned extracts. Table 3 presents the range of MBCs of those six propolis extracts which were serially diluted in a tube [60].

Uzel et al. [61] determined the antimicrobial effect of four various Anatolian propolis samples on different groups of microorganisms, e.g., *S. mutans* and *S. sobrinus*, and the researchers compared their chemical compositions. The authors determined MIC values and the chemical compositions of EEPs. The MIC values of the most effective propolis are shown in Table 3. The GC-MS analysis indicated that the chief compounds of four Anatolian propolis samples are flavonoids such as pinocembrin, pinostrobin, isalpinin, pinobanksin, quercetin, naringenin, galangin, and chrysin [61].

Bruschi et al. [62] evaluated the antimicrobial activity of propolis against *S. salivarius*, *S. sanguinis*, *S. mitis*, *S. mutans*, *S. sobrinus*, and *L. casei*. The authors noticed that propolis possesses antimicrobial activity against all the strains of bacteria that were investigated. The determination of the MIC results showed that *S. sanguinis* and *S. mitis* were more susceptible to the propolis (Table 3) [62].

De Paula et al. [63] investigated the antimicrobial activity of ethanolic extract and fractions of Brazilian green propolis (BGP) collected by bees from *Baccharis dracunculifolia*. The results indicated that *S. mutans*, *S. sobrinus*, *P. gingivalis*, *F. nucleatum*, *F. necrophorum*, and *A. actinomycetemcomitans* were susceptible to BGP (Table 3). Antimicrobial activity was evaluated by MIC, MBC, and the inhibition zone. Inhibition zones were 18.3 ± 1.15 , 28.6 ± 0.57 , 14.0 ± 0.00 , 15.2 ± 0.26 , 17.3 ± 0.57 , and 14.6 ± 0.57 mm, respectively. None of the assayed fractions (coumaric acid, kaempferol, pinobanskin-3-acetate, chrysin, galangin, kaempferide, and artepillin C) was found to be more active than the extract. Thus, it can be concluded that the antimicrobial activity results from a synergistic effect of propolis constituents [63].

The antimicrobial activity of propolis ethanolic extracts from Iran-Turanian, European-Siberian, Brazil, and Turkey against certain oral pathogens was analyzed by Koru et al. [19]. Nine different strains were analyzed: *P. anaerobius*, *P. micros*, *P. oralis*, *P. melaninogenica*, *P. gingivalis*, *F. nucleatum*, *V. parvula*, *L. acidophilus*, and *A. naeslundii*. The propolis extracts from Rize (17.5% w/v), Kazan (9.4% w/v), Mugla (13.6% w/v), Tahtakopru (5.8% w/v), and Brazil (4.6% w/v) were analyzed. The Kazan propolis sample showed significantly lower MIC values in comparison to other samples. The obtained MIC values are shown in Table 3. Moreover, the microorganisms died within 4 h (*P. anaerobius*, *P. micros*, *L. acidophilus*, and *A. naeslundii*), 8 h (*P. oralis*, *P. melaninogenica*, and *P. gingivalis*), 12 h (*F. nucleatum*), and 16 h (*V. parvula*) of incubation. The researchers did not identify any viable cells (CFU) after the above-listed periods of time [19].

The antimicrobial effect of Cretan propolis against *S. mutans* was investigated by Popova et al. [64]. The researchers observed a 20 mm inhibition zone for *S. mutans* after ethanolic propolis extract treatment. Moreover, the MIC value was calculated to be 0.17 mg/mL. The observed effect was weaker than in case of sanguinarine used as the control (28 mm inhibition zone, MIC = 0.0015 mg/mL) [64].

Kim et al. [65] determined the optimal concentration of Korean propolis against *S. mutans* and *S. sobrinus* isolated from Koreans. A dry extract of propolis was obtained and dissolved in ethanol at a concentration of 448 mg/mL. The researchers found out that propolis at a concentration of 35 µg/mL could be used *in vivo* to prevent the development of dental caries. The determination of the MIC was used to obtain those results. After 24 h of incubation in appropriate conditions, the researchers adopted the lowest concentration of ethanol propolis solution which was required to inhibit visible growth as MIC (Table 3) [65].

Liberio et al. [66] researched the antimicrobial activity of *M. fasciculata* geopropolis against oral pathogens, its effects on *S. mutans* biofilms, and the chemical composition of the extracts. Moreover, the researchers investigated a gel for whose preparation a geopropolis extract was used to evaluate its effectiveness against *S. mutans* as well as its immuno-toxicological potential. The researchers concluded that geopropolis would exhibit antimicrobial activity against *S. mutans*. The agar diffusion method and the broth dilution technique were employed to assess antimicrobial activities of three hydroalcoholic extracts (HAEs) of geopropolis, and hexane and chloroform fractions of one extract. Ethanol (70%, v/v) and chlorhexidine (0.12%, w/w) were used as negative and positive controls, respectively. Inhibition zones ranging from 10 to 13 mm in diameter for *S. mutans*, and no activity against *L. acidophilus* were detected in case of HAE-2 and HAE-3. The average of MBCs for HAE-2, its chloroform fraction, and HAE-3 against *S. mutans* are presented in Table 3. What is more, HAE-2 had bactericidal effects on *S. mutans* biofilms after 3 h of treatment. The total concentrations of phenol and flavonoid were significantly different in various samples [66].

The ethanolic and aqueous extracts of the Iranian propolis collected in the northeast area of Tehran were used to evaluate propolis antimicrobial activity against *S. mutans*, *S. salivarius*, and *L. casei*. The study was conducted by Jafarzadeh Kashi et al. [15]. It could be concluded that the ethanolic extract of Iranian propolis is effective when oral biofilms and subsequent dental caries development need to be controlled. The zones of growth inhibition, MIC, and MBC were measured. The inhibition zones were

16.00 ± 0.00, 20.00 ± 1.00, and 12.00 ± 1.00 mm (ethanolic extract of propolis) for *S. mutans*, *S. salivarius*, and *L. casei*, respectively, and 12.00 ± 1.00 mm (water extract of propolis) for *S. mutans*. The obtained results showed that the ethanolic extract had bacteriostatic and bactericidal activity against all the strains (Table 3). On the other hand, the aqueous extract was bactericidal only against *S. mutans* [15].

Kousedghi et al. [67] compared the activity of calcium hydroxide and propolis against *Lactobacillus spp.* They carried out an experimental study in order to assess the antimicrobial activity of ethanol extract of propolis and calcium hydroxide (Ca(OH)₂) powder mixed with saline solution. The diameter of the inhibition zone, MIC, and MBC was determined. The authors indicated that propolis was more effective against *Lactobacillus spp.* with 8.42 mm compared with the 7.0 mm mean diameter of the inhibitory zone for Ca(OH)₂. In addition, the MIC and MBC values of propolis were lower than those of calcium hydroxide (Table 3) [67].

Mohammad [31] determined the antibacterial actions of aqueous propolis extract against black pigmented *P. gingivalis* (from periodontal pockets). The results indicated that propolis had antibacterial actions against *P. gingivalis*, and it might be employed to treat periodontal diseases. Additionally, it can be one of substances beneficial for prophylactic procedures. These results were obtained based on a study in which swabs taken from the periodontal pockets of 30 patients were used. The antimicrobial activity of propolis by the well-diffusion method was characterized by inhibition zones. At 50% concentration of propolis, the inhibition zone was 30 mm [31].

The antimicrobial activities of neovestitol and vestitol isolated from Brazilian red propolis (BRP) were evaluated by Bueno-Silva et al. [68]. The results indicated that propolis can be useful in pharmaceutical treatment due to its antimicrobial activities. These results were obtained based on evaluating MIC and MBC against *S. mutans*, and *S. sobrinus*. The obtained MIC and MBC values of ethanol propolis extract (EEP) are presented in Table 3 [68].

Guilherme da Cunha et al. [69] studied the antimicrobial properties of the ethanolic extract of geopropolis (EEGP) against *S. mutans* and *A. naeslundii*. EEGP was collected by *Melipona scutellaris*. The authors evaluated also the antiproliferative activity of EEGP and its bioactive fraction. MIC and MBC were determined to analyze the antimicrobial activity of EEGP and fractions, and the results are presented in Table 3. This suggests that geopropolis may be a good source of antibiofilm agents as well as possesses antimicrobial activity [69].

Dziedzic et al. [70], in their ex vivo study, examined the antibacterial properties of ethanol extract of propolis (EEP) against cariogenic bacteria: salivary *S. mutans* and *Lactobacillus spp.* The samples were collected in Poland. The results showed that the extract of Polish propolis affected salivary *S. mutans* and *Lactobacillus spp.* viability, exhibiting an antibacterial efficacy on them, while *Lactobacillus spp.* were more susceptible to EEP. The authors estimated MIC and MBC values (Table 3). The results they obtained suggest that antibacterial substances with propolis could locally affect cariogenic bacteria [70].

Speciale et al. [71] tested the *in vitro* activity of alcoholic and hydroglyceric extract of propolis against *S. pyogenes*. The authors also evaluated the *in vitro* activity of a combination of propolis and its active ingredients (galangin, pinocembrin, chrysin, quercetin, caffeic acid phenethyl ester, ferulic acid phenethyl ester, and farnesol) and some beta-lactams, macrolides, and fluoroquinolones. The results did not demonstrate a synergistic activity between antibiotics, propolis, and its constituents. The obtained MIC value of propolis hydroglyceric extract for *S. pyogenes* is presented in Table 3 [71].

Barrientos et al. [72] used propolis samples from Chile to determine their chemical and botanical characteristics. The authors evaluated how *S. mutans* and *S. sobrinus* are biologically affected by propolis. Beekeepers from the central and southern regions of Chile supplied twenty propolis samples for testing. The MIC was determined on *S. mutans* and *S. sobrinus*. In all propolis samples, mainly structures from native plant species were

detected. A wide spectrum of action was recorded, although the growth of *S. mutans* was inhibited by all propolis samples (Table 3) [72].

Da Silva et al. [73] evaluated *in vitro* the synergistic effect between the ethanol extract of different Brazilian propolis samples: green (*Baccharis dracunculifolia*) (A), red (*Dalbergia ecastophyllum*) (B), and brown (*Copaifera sp.*) (C) propolis by the antimicrobial sensitivity of *S. mutans* and *S. sanguinis*. The results showed that all extracts inhibited the growth of both microorganisms. These results were obtained based on measuring inhibition zones after 24 h and 48 h. The inhibition zones after 24 h were 21.50 ± 0.50 (A), 27.25 ± 0.25 (B), 21.00 ± 0.0 mm (C) for *S. mutans*, and 16.67 ± 1.09 (A), 19.33 ± 0.94 (B), 15.67 ± 0.19 mm (C) for *S. sanguinis*, respectively. The inhibition zones after 48 h were 21.50 ± 0.50 (A), 27.25 ± 0.25 (B), and 21.00 ± 0.0 mm (C) for *S. mutans*, and 16.67 ± 1.00 (A), 19.33 ± 0.94 (B), and 15.67 ± 0.19 mm (C) for *S. sanguinis*, respectively [73].

Hatunoğlu et al. [74] investigated how the antibacterial and mechanical properties of conventional glass ionomer cement (GIC), used in orthodontic band cementation, would be affected by ethanolic extracts of propolis (EEP). Four types of GIC were analyzed: one using the original composition (without EEP) and three with addition EEP (10, 25, and 50%). The authors showed that EEP in concentrations of 25 and 50% inhibited the growth of *S. mutans*, while EEP in the concentration of 10% and control group showed no impact on *S. mutans*. The obtained MIC values for EEP are presented in Table 3. Interestingly, the MIC values for GIC and EEP were much higher ($31.2 \mu\text{g/mL}$ for GIC + 50% EEP, $125 \mu\text{g/mL}$ for GIC + 25% EEP, and $>1000 \mu\text{g/mL}$ for GIC + 10% EEP) than those for EEP only. It suggests that EEP possesses much better antibacterial activity toward *S. mutans* [74].

De Luca et al. [75] added to a chitosan polymeric base (CHV), ethanolic propolis extract in various concentrations of propolis varnishes (PV): PV1 (5%), PV2 (10%), and PV3 (15%). The researchers could conclude that the antimicrobial properties of propolis were maintained even when propolis was incorporated into the coating of chitosan. The authors indicated that the antimicrobial activity of propolis varnishes against *S. mutans*, *S. sanguinis*, *S. salivarius*, and *L. casei*. The MIC and MBC values are presented in Table 3 [75].

Ophori et al. [76] examined whether upper respiratory tract infections (URTIs) could be treated and controlled with the use of propolis due to its antibacterial activity. The results proved the antimicrobial effectiveness of propolis when used for the treatment and management of bacterial URTI. In this study, propolis extract was obtained with 70% ethanol, and serial dilutions of 0.25, 0.5, 1, 2, 4, 8, and $10 \mu\text{g/mL}$ were prepared. A total of 250 throat swabs were collected from patients (aged between 15 and 30 years) diagnosed with URTI. Only 2% had positive cultures with *S. pyogenes*. The results showed that these isolates were sensitive to propolis at all concentrations. The inhibition zone for *S. pyogenes* was 10 mm, while the MIC value is presented in Table 3 [76].

The antimicrobial activity of propolis toothpaste and mouth rinse against supragingival multispecies biofilm was analyzed by Vanni et al. [43]. The biofilm contained *A. naeslundii*, *V. dispar*, *F. nucleatum*, *S. mutans*, and *S. oralis*. The authors tested toothpaste without propolis, toothpaste with propolis (0.9%), toothpaste with chlorhexidine (0.12%), mouth rinse with propolis (10%), mouth rinse with chlorhexidine (0.12%), and saline solution. The obtained colony-forming units (CFU) values were 5.14×10^7 and 3.94×10^7 , and 6.49×10^7 , respectively for toothpaste without propolis, with propolis, and with chlorhexidine. In case of mouth rinse, the CFU values were 3.77×10^8 and 4.58×10^6 , respectively, for mouth rinse with propolis and chlorhexidine. Interestingly, the CFU for the control sample (saline solution) was 3.36×10^8 [43].

Ethanolic extract of propolis and 0.2% chlorhexidine gluconate against oral pathogens were analyzed for their antibacterial activity by Akca et al. [77]. The propolis extract similar to chlorhexidine inhibited all of the oral microorganisms (*S. mutans*, *S. sobrinus*, *L. acidophilus*, *L. salivarius subsp. salivarius*, and *A. israelii*) except *P. gingivalis* and *A. actinomycetemcomitans*. Interestingly, the extract was also more effective against *P. intermedia* than chlorhexidine. The obtained MIC and MBC values are presented in Table 3. The effect of propolis extract was not caused by adding 80% ethanol, since all strains were resistant to the ethanol [77].

The antimicrobial activity of Brazilian green wild propolis against *S. mutans* dental biofilm was analyzed by Cardoso et al. [78]. Four different groups of compounds for biofilm treatment (30 mL/1min, for 5 days) were tested: 33.3% ethanol propolis extract, 0.12% chlorhexidine digluconate, 80% ethanol, and Milli-Q water. Each compound significantly reduced the percentage of hardness loss. The obtained CFU/biofilm values for *S. mutans* were 7.26 ± 0.08 , 6.79 ± 0.10 , 8.00 ± 0.05 , and 8.29 ± 0.17 , respectively, for ethanol propolis extract, chlorhexidine, ethanol, and water [78].

The antimicrobial activity of propolis from Turkey against *S. mutans* and *S. salivarius* was analyzed by Ertürk et al. [79]. The authors used ethanol, ethyl acetate, acetone, water, DMSO, and methanol extract of propolis. The obtained MIC values of *S. salivarius* were $1 \leq$, $2 \leq$, and $2 \leq$ mg/mL, respectively, for ethyl acetate, acetone, and methanol extract. In case of *S. mutans*, the MIC values were $4 \leq$, $1 \leq$, $4 \leq$, $2 \leq$, and $4 \leq$ mg/mL, respectively, for ethyl acetate, ethanol, acetone, methanol, and DMSO extract [79].

The antibacterial activity of Brazilian green propolis (BGP) against oral pathogens (*S. mutans*, *S. sanguinis*, *P. gingivalis*, and *A. actinomycetemcomitans*) was analyzed by Oda et al. [80]. The results indicated that BGP has antibacterial properties. The study showed that Brazilian propolis in the concentration of 500 µg/mL significantly decreased the growth of *S. mutans*, while the concentration of 2000 µg/mL resulted in total inhibition. In case of *S. sanguinis*, a significant decrease was observed after treatment with Brazilian propolis (50 µg/mL), while the complete growth inhibition was in the concentration of 200 µg/mL. Unfortunately, Brazilian propolis was less effective against *A. actinomycetemcomitans*, since in the concentration of 2000 µg/mL, the growth was still observed. In case of *P. gingivalis*, the propolis effect depended on the species (W83 and ATCC33277). The obtained results showed that in case of W83, a substantial reduction in growth was recorded for the propolis concentration of 50 µg/mL, and the total growth inhibition was observed in the propolis concentration of 200 µg/mL, while for ATCC33277, it was 100 and 400 µg/mL, respectively [80].

The antimicrobial effect of 10% (*w/v*) ethanol extract of Indian propolis against *S. pyogenes* was analyzed by Souza et al. [81]. The inhibition zone of the extract for *S. pyogenes* was 16 ± 2 mm [81].

The antimicrobial activity of seven different types of South Brazilian organic propolis samples (OP1-OP7) against *S. mutans*, *S. oralis*, and *S. sorbinus* was analyzed by Tiveron et al. [82]. Interestingly, OP2 showed the lowest MIC value for *S. sorbinus*, OP1 and OP3 showed the lowest MIC value for *S. oralis*, and OP1-OP4 showed the lowest MIC value for *S. mutans*. In case of MBC, the lowest values presented OP1 and OP7 for *S. mutans*, OP1, OP2, and OP7 for *S. oralis*. These values are shown in Table 3. It is worth observing that all variants of propolis inhibited *S. mutans* biofilm formation at the concentrations of 400 and 800 µg/mL for approximately 90%. OP5 significantly inhibited biofilm formation at 400 µg/mL, while OP5 and OP6 in the concentration of 200 µg/mL were not effective in biofilm inhibition. OP2 and OP3 showed the highest effectiveness for biofilm inhibition at about 50 and 60%, respectively, in the concentration of 100 µg/mL [82].

The antibacterial activity of NBF gel containing vitamin C, E, and propolis against *S. mutans* was examined by Abbas et al. [83]. The study showed a concentration-dependent rise in the inhibition zone from 2.3 ± 1.7 to 16.5 ± 3.1 mm and from 4.3 ± 3.6 to 13.8 ± 2.8 mm, respectively, for alcoholic and aqueous extracts. The authors used alcoholic and aqueous extracts in the concentration range from 10 to 50%. In the lowest concentration (10%), the inhibition zone was not detected, while in the concentration of 20%, the inhibition zone occurred only in the alcoholic extract. The study also demonstrated that the inhibition zone decreased with increasing the duration of use of the appliance. Moreover, the authors observed that the mean of the colony count increased with the increasing time of incubation [83].

The antimicrobial activity of Czech, German, and Irish ethanol propolis extract and aqueous German propolis extract against *S. oralis* and *S. pyogenes* were analyzed by AL-Ani et al. [84]. Interestingly, the Irish and Czech propolis was most efficient against

S. oralis and *S. pyogenes*, while German aqueous propolis extract was less efficient. The authors calculated MIC and MBC values (Table 3). Moreover, the authors analyzed also the impact of Irish ethanol propolis extract and vancomycin in a checkerboard assay. In the checkerboard assay, synergistic interaction against *S. pyogenes* of ethanol or aqueous extracts of propolis with antibiotics was shown [84].

The antibacterial action of 10% propolis ethanol tincture against *S. gordonii*, *S. sanguinis*, *S. mutans*, *S. sobrinus*, *L. acidophilus*, and *A. naeslundii* was evaluated by Habluetzel et al. [36]. The erosion study in which one hundred and twenty human enamel specimens were covered with a salivary pellicle and modified with propolis, then eroded with 1% citric acid (pH 3.6 for 2 min), showed that propolis did not cause enamel erosion. In the microbiological assay, MIC values were calculated, and they are presented in Table 3. No antimicrobial activity was detected in case of ethanol (10%). Moreover, the adhesion study showed that 30 minutes and 2 hours of treatment with propolis significantly reduces the adherence of *S. gordonii* [36].

The effect of red propolis hydro-alcoholic extract on *S. mutans* biofilm formation was evaluated by Martins et al. [85]. The obtained MBC value (1171.87 µg/mL) was about four times higher than the MIC value (292.97 µg/mL). Chlorhexidine showed bactericidal activity against *S. mutans* in the concentration range from 0.15 to 300 µg/mL. Moreover, a bigger number of colony-forming units was detected in 3% propolis extract in comparison to 0.12% chlorhexidine extract. The researchers did not record significant differences between the group that received inoculum (3% red propolis extract, 0.85% NaCl, 0.05% NaF, and 0.12% chlorhexidine) and 0.12% chlorhexidine only as long as the forming of a mature biofilm on the surface of enamel blocks is concerned. Moreover, the insoluble extracellular polysaccharide (IEPS) that prevailed over soluble (SEPS) was significantly lower in the group that used red propolis and chlorhexidine when compared with the negative control. The 3% propolis extract effectively reduces *S. mutans* colonization, impairing the production of soluble and insoluble extracellular polysaccharides, and it reduces dental enamel demineralization, which suggests that propolis can be effective in anti-cariogenic effect [85].

The effect of Korean propolis ethanol extract from six different regions against *S. mutans* was analyzed by Roh and Kim [86]. All of the samples reduced microbial growth. The results showed that propolis collected from the regions Uijeongbu and Sangju were the most effective against *S. mutans*. The authors analyzed two concentrations of propolis extract (10 and 50 mg/mL). The obtained results of the inhibition zone were from 8.07 ± 0.21 to 9.10 ± 0.17 mm for propolis (10 mg/mL) and from 9.33 ± 0.38 to 10.88 ± 0.39 mm for propolis (50 mg/mL), dependently on the region of origin [86].

The antibacterial activity of propolis mouthwash against *S. mutans* was analyzed by Santiago et al. [87]. The determination of MIC was used to estimate the product's antibacterial properties and its effectiveness against *S. mutans in vitro*. The obtained MIC value for propolis is presented in Table 3. The MIC value for chlorhexidine was 5 µg/mL. Ethanol as a solvent did not show any impact on the activity of propolis extract. Moreover, the mixture of 1.3% propolis with 0.06% chlorhexidine showed inhibitory activity against *S. mutans* even with the use of a 64-fold dilution to the ultimate chlorhexidine concentration (9.5 µg/mL) [87].

The antibacterial activity of 6.5% Iranian propolis ethanol extract against *S. mutans* and *S. salivarius* was analyzed by Asgharpour et al. [34]. They analyzed 57 *Streptococcus spp.* strains: *S. salivarius* (n = 20), *S. mutans* (n = 20), *S. oralis* (n = 3), *S. mitis biovar 1* (n = 4), *S. uberis* (n = 5), *S. bovis* (n = 3), *S. equinus* (n = 1), and *S. parasanguinis* (n = 1). The results indicate that Iranian propolis inhibits cariogenic bacteria and oral biofilm formation, and it is not cytotoxic for normal cells; thus, it can be a promising complementary medicine. In case of Iranian propolis extract, the lowest MIC has *S. salivarius*. The obtained MIC values depend on the strain and were one to five times lower than the MBC values (Table 3). The sub-MIC concentrations significantly decreased the biofilm growth after 24 h treatment. The most effective were Iranian propolis extract (6 µg/mL) and quercetin (20 µg/mL). The maximum biofilm reduction was 71 to 76% and 44 to 56%, respectively, for propolis

extract and quercetin, depending on the used method. The results indicated a much greater efficiency of the extract than the one of quercetin [34].

The impact of 5% Peruvian propolis ethanolic extract on *S. mutans* growth was analyzed by Becerra et al. [88]. The results indicated that Peruvian propolis extract possesses better antimicrobial activity than chlorhexidine digluconate. The negative control was 96% ethanol, while the positive control was 0.12% chlorhexidine digluconate. The inhibition growth area after the propolis treatment was 18.2 ± 1.8 and 26.4 ± 2.6 mm for summer and autumn samples, respectively. The inhibition area for chlorhexidine was 13.0 mm. The growth of *S. mutans* was not inhibited by the negative control [88].

The antibacterial activity of Italian propolis against *S. pyogenes* was investigated by Governa et al. [89]. The study showed that propolis is an effective antimicrobial agent. The authors used ethanol extract. The obtained MIC value was 156 $\mu\text{g}/\text{mL}$ and the effect was not influenced by the ethanol (MIC 100–125 $\mu\text{g}/\text{mL}$) [89].

The antibacterial activity of mouthwash containing 0.8% of Brazilian red propolis extract against *S. mutans*, *S. sanguinis*, *S. salivarius*, and *L. casei* was analyzed by Martins et al. [14]. The study showed that red propolis can be a natural alternative in bacterial infection, since it possesses antibacterial activity against *Streptococcus spp.* and *L. casei* as well as a similar cytotoxicity and antibiofilm effect in comparison to chlorhexidine. The authors analyzed MIC and MBC of 0.05% sodium fluoride (NaF); 0.8% red propolis extract (RPE); 0.8% RPE + 0.05% NaF, and 0.12% chlorhexidine containing mouthwash. The results are shown in Table 3. The analysis of antimicrobial activity showed also that using RPE mouthwash resulted in highly reduced viable microorganisms (7.74 $\text{Log}_{10}\text{CFU}/\text{mL}$) in comparison to RPE+NaF (7.95 $\text{Log}_{10}\text{CFU}/\text{mL}$), chlorhexidine (7.93 $\text{Log}_{10}\text{CFU}/\text{mL}$), and the ordinary mouthwash. The greatest effectiveness in reducing *Streptococcus spp.* was found for chlorhexidine, which did not vary from RPE and RPE+NaF [14].

Nazeri et al. [90] determined the antimicrobial activity of Iranian propolis against *S. mutans* and *L. acidophilus*. MIC values are presented in Table 3. Moreover, the researchers observed a rise in bacterial levels in water, which suggests that water did not decrease the number of both bacteria. In case of *L. acidophilus*, propolis most significantly reduced the number of bacteria (from 6.14 to 5.35, 5.68, and 5.97, after 12 hours, 1 week, and 2 weeks, respectively). Listerine and chlorhexidine (0.12%) reduced the number of bacteria, but after 1-week treatment, they reached the baseline level. Regarding *S. mutans*, propolis most significantly reduced the number of bacteria (from 4.15 to 3.37, 3.81, and 4.05, after 12 hours, 1 week, and 2 weeks, respectively). Listerine and chlorhexidine reduced the number of bacteria, but after 2 weeks of treatment, they reached the baseline level. Thus, propolis was more efficient than other mouthwashes [90].

Agbor et al. [91] analyzed the impact of propolis extracts from the western region of Cameroon on *Lactobacillus spp.* and *S. mutans*. They proved that an inhibition diameter was greater for the aqueous extract of propolis than the one for the hydroalcoholic extract. The authors used hydroalcoholic and aqueous extracts of propolis as well as gentamycin to determine MIC and MBC. Table 3 presents the obtained results. The inhibition diameters of extracts on *S. mutans* corresponding to MICs were 10, 26, and 8 mm, respectively for aqueous, gentamycin, and hydro alcoholic extract. In case of *Lactobacillus spp.* the inhibition diameters were 11, 29, and 8 mm, respectively, for aqueous, gentamycin, and hydroalcoholic extract. The authors suggest that the difference between the aqueous and hydro alcoholic extract may be caused by the fact that the chemical components may vary, and resin-like substance may be present. The chemical analysis of both extracts showed that the aqueous extract is characterized by higher concentration of metabolites (coumarins, saponins, alkaloids, tannins, quinones, and flavonoids) than the hydroalcoholic extract [91].

Rivero-Cruz et al. [92] studied the antibacterial properties of the ethanolic extract of propolis (EEP), and they used samples from México. MIC assay was employed to test the compounds which were isolated. The antimicrobial screening revealed that EEP inhibited the growth of *S. mutans*, *S. oralis*, *S. sanguinis*, and *P. gingivalis*. MIC values are presented in Table 3 [92].

The antibacterial effect of Iranian propolis and Persica mouthwashes against *S. mutans*, *S. salivarius*, and *S. sanguis* was analyzed by Alemrajabi et al. [93]. The results indicated that the propolis sample exhibited much better antibacterial activity in comparison to Persica mouthwash. These results were obtained based on the inhibition zone and MIC determination. The zone of inhibition was 7.8 ± 0.2 , 14.0 ± 2.7 and 12.2 ± 0.1 mm, respectively for *S. mutans*, *S. salivarius*, and *S. sanguis*. It suggests that *S. salivarius* was significantly more sensitive in comparison to other strains. In case of Persica mouthwash, the most sensitive was also *S. salivarius* with the inhibition zone 24.0 ± 2.16 mm. The obtained MIC values for propolis are presented in Table 2. The obtained MIC values for Persica mouthwash were 1.4, 1.4, and 1.8 $\mu\text{g}/\text{mL}$, respectively for *S. mutans*, *S. salivarius*, and *S. sanguis* [93].

Bapat et al. [94] assessed the antimicrobial activity of the aqueous and ethanol extracts of propolis. The MIC values for *S. mutans* and *L. acidophilus* are presented in Table 3. In conclusion, this study determined propolis as an effective agent against oral pathogens *S. mutans* and *L. acidophilus* [94].

The antimicrobial effect of thirteen different Peruvian propolis against *S. gordonii* and *F. nucleatum* was analyzed by Gómez et al. [95]. Here, 0.12% chlorhexidine was used as a control. The authors noticed that *S. gordonii* was resistant to four samples of propolis and *F. nucleatum* was resistant to seven samples of propolis. The obtained inhibition zones for chlorhexidine were 14.45 ± 0.30 and 14.40 ± 0.18 mm, respectively, for *S. gordonii* and *F. nucleatum*. In case of propolis samples, the inhibition zones were from 1.73 ± 0.15 to 10.88 ± 0.09 mm and 7.65 ± 0.10 to 10.88 ± 0.10 mm, respectively, for *S. gordonii* and *F. nucleatum* [95].

The antibacterial effect of propolis gel on *S. mutans* and *L. acidophilus* was evaluated by Hajiahmadi et al. [96]. The obtained results showed that in all concentrations, propolis and *Aloe vera* gel inhibited the growth of *S. mutans* and *L. acidophilus*. The inhibition of *Lactobacillus* was stronger than *Streptococcus*. The inhibition zone for propolis gel were 8.05 ± 0.27 , 11.50 ± 0.74 , and 14.26 ± 0.77 mm (for *L. acidophilus*) and 7.74 ± 0.51 , 8.85 ± 1.03 , and 10.81 ± 0.70 mm (for *S. mutans*), respectively, after 24, 48, and 72 h. It is worth noting that the inhibition area of lower concentrations of propolis and *Aloe vera* gel was bigger than the one of other analyzed gels. This suggests the antibacterial effectiveness of a gel with propolis and *Aloe vera* even at low concentrations [96].

Ismail et al. [97] evaluated the antimicrobial activities of ethanol extracts of propolis (EEP) from *Trigona thoracica* against *S. mutans* and *S. sobrinus*. The results showed that the tested propolis can be used as an antibacterial agent against investigated cariogenic bacteria. The antimicrobial activity of EEP expressed as the mean of inhibition diameter as well as MIC values were determined. The median inhibition diameter zone using EEP against *S. mutans* and *S. sobrinus* was 14 and 18 mm, respectively. The obtained MIC values of EEP against *S. mutans* and *S. sobrinus* are presented in Table 3 [97].

Navarro-Perez et al. [98] investigated the antimicrobial effect of Spanish ethanolic extract of propolis against *S. mutans* and *S. sanguinis*. The obtained results showed that Spanish propolis is effective against *S. mutans* and *S. sanguinis*, which play a crucial role in dental plaque formation. The authors determined the MIC and MBC values, which are presented in Table 3. The ethanol used in the extract had no impact on microbial viability, since a minimum 12.5% concentration was necessary to inhibit the growth of the analyzed strains. The MIC values for ampicillin sodium (positive control) were 0.16 and 0.31 $\mu\text{g}/\text{mL}$, while MBC values were 0.08 and 0.31 $\mu\text{g}/\text{mL}$, respectively, for *S. mutans* and *S. sanguinis*. The analyzed propolis extract does not possess as strong antimicrobial activity as ampicillin sodium. *S. sanguinis* is more susceptible to the propolis extract in comparison to *S. mutans* [98].

Ozan et al. [99] researched the antimicrobial effect of propolis drops on *S. mutans*. The authors analyzed seven different drops: Umay Herbal Organic Propolis, Bee'o Up (15%), Propoli EVSP, Brazilian Green Liquid Propolis, Eğriçayır Propolis, Bee'o Up (30%), Biostore Propolis as well as 2% chlorhexidine and 10 μL of chloramphenicol as a positive

control. The obtained minimal area of zones for *S. mutans* was: 0, 20, 14, 15, 30, 24, 12, 34, and 22 mm, respectively, for Umay Herbal Organic Propolis, Bee' o Up (15%), Propoli EVSP, Brazilian Green Liquid Propolis, Eğriçayır Propolis, Bee' o Up, Biostore Propolis, 2% chlorhexidine, and chloramphenicol. Interestingly, Eğriçayır Propolis and Bee' o Up showed stronger activity than chloramphenicol, while chlorhexidine showed the strongest impact against *S. mutans* [99].

Tambur et al. [7] studied the antimicrobial activities of propolis solutions against some oral cariogenic (*S. mutans*, *S. mitis*, *S. sanguis*, and *L. acidophilus*) and periodontopathic bacteria (*A. odontolyticus*, *E. corrodens*, and *F. nucleatum*). Their results indicate that propolis may help prevent dental caries and other oral infectious diseases. The authors investigated the antimicrobial activity of propolis dissolved in benzene, diethyl ether, and methyl chloride by the agar dilution method. Dilutions for propolis were 50, 25, 12.5, and 6.3 µg/mL of active propolis solutions. The results showed that propolis solutions dissolved in benzene, diethyl ether, and methyl chloride demonstrated equal effectiveness against all investigated oral bacteria. However, propolis solution dissolved in acetone displayed a lower MIC value only for *L. acidophilus* (Table 3) [7].

Finally, the studies performed by Onur et al. [100] showed that MIC and MBC values of water-based Turkish propolis extract against *L. acidophilus* were 5000 µg/mL (ppm) [100].

Table 3. Summary of antibacterial activity of different propolis extracts.

Bacteria	MIC	MBC	Reference
<i>Actinomyces naeslundii</i>	51.2 + 44.4 µg/mL *	89.6 + 98.1 µg/mL *	[19]
	800–1600 µg/mL	>1600 µg/mL	[69]
	≤0.63%		[36]
<i>Actinomyces odontolyticus</i>	12.5 µg/mL		[7]
<i>Aggregatibacter actinomycetemcomitans</i>	30–60 µg/mL	200–400 µg/mL	[63]
	64 µg/mL	128 µg/mL	[77]
<i>Eikenella corrodens</i>	12.5 µg/mL		[7]
<i>Fusobacterium necrophorum</i>	30–60 µg/mL	200–400 µg/mL	[63]
<i>Fusobacterium nucleatum</i>	256.0 + 147.8 µg/mL *	358.4 + 132.1 µg/mL *	[19]
	30–60 µg/mL	200–400 µg/mL	[63]
	12.5 µg/mL		[7]
<i>Lactobacillus acidophilus</i>	48.8 + 46.8 µg/mL *	68.8 + 54.8 µg/mL *	[19]
	4.0 µg/mL	4–8 µg/mL	[77]
	≤0.63%		[36]
	600 µg/mL		[90]
	12.5 µg/mL (propolis solutions dissolved in benzene, diethyl ether and methyl chloride) 6.3 µg/mL (propolis solutions dissolved in acetone)		[7]
4.5 µg/mL (cold ethanolic propolis) 5 µg/mL (hot ethanolic propolis)		[94]	
	5000 µg/mL	5000 µg/mL	[100]

Table 3. Cont.

Bacteria	MIC	MBC	Reference
<i>Lactobacillus casei</i>	200–300 µg/mL		[62]
	250 µg/mL (ethanol extract)	250 µg/mL (ethanol extract)	[15]
	29.76 mg/mL	59.52 mg/mL	[14]
	0.6–1.2 mg/mL	0.6–1.2 mg/mL	[75]
<i>Lactobacillus salivarius</i> subsp. <i>salivarius</i>	2.0 µg/mL	4.0 µg/mL	[77]
<i>Lactobacillus</i> spp.	8.0 mg/mL	16 mg/mL	[67]
	50 mg/mL (aqueous extract) 100 mg/mL (hydroalcoholic extract)	25 mg/mL (aqueous extract)	[91]
	0.7 mg/mL	5.91 mg/mL	[70]
<i>Peptostreptococcus anaerobius</i>	20.8 + 10.1 µg/mL *	32.0 + 18.4 µg/mL *	[19]
<i>Peptostreptococcus micros</i>	16.0 + 9.2 µg/mL *	19.2 + 11.4 µg/mL *	[19]
<i>Porphyromonas gingivalis</i>	30–50 µg/mL	200–400 µg/mL	[63]
	294.4 + 198.2 µg/mL *	384.0 + 170.6 µg/mL *	[19]
	32 µg/mL	64 µg/mL	[77]
	500 µg/mL		[92]
<i>Prevotella intermedia</i>	8.0 µg/mL	8.0 µg/mL	[77]
<i>Prevotella melaninogenica</i>	204.8 + 66.0 µg/mL *	381.6 + 132.1 µg/mL *	[19]
<i>Prevotella oralis</i>	230.4 + 54.0 µg/mL *	460.8 + 107.9 µg/mL *	[19]
<i>Streptococcus bovis</i>	12.5 µg/mL	50 µg/mL	[34]
<i>Streptococcus cricetus</i>	25 µg/mL (EEP BA), 50 µg/mL (EEP RS), 400 µg/mL (EEP MG)	100 µg/mL (EEP BA), 200 µg/mL (EEP RS), >800 µg/mL (EEP MG)	[21]
<i>Streptococcus equinus</i>	12.5 µg/mL	100 µg/mL	[34]
<i>Streptococcus gordonii</i>	1.25%		[36]
<i>Streptococcus mitis</i>	20 µg/mL		[62]
	12.5 µg/mL		[7]
<i>Streptococcus mitis</i> biovar 1	6.25–12.5 µg/mL	50 µg/mL	[34]
<i>Streptococcus mutans</i>	50 µg/mL (EEP BA), 100 µg/mL (EEP RS), 400 µg/mL (EEP MG)	400 µg/mL (EEP BA), 400 µg/mL (EEP RS), >800 µg/mL (EEP MG)	[21]
	50–100 µg/mL	800–1600 µg/mL	[59]
		2.5–10 mg/mL	[60]
	8.0 µg/mL		[61]
	200 µg/mL		[62]
	25–50 µg/mL	200–400 µg/mL	[63]
	100–200 µg/mL	100–200 µg/mL	[68]
	0.17 mg/mL		[64]
	25–50 µg/mL	>1600 µg/mL	[69]
	35 µg/mL		[65]
1.10 mg/mL	9.01 mg/mL	[70]	

Table 3. Cont.

Bacteria	MIC	MBC	Reference
<i>Streptococcus mutans</i>		11.12 mg/mL	[66]
	250 µg/mL (ethanol extract) 500 µg/mL (water extract)	250 µg/mL (ethanol extract) 20 mg/mL (water extract)	[15]
	4.0 µg/mL	8.0 µg/mL	[77]
	50–100 µg/mL (OP1–OP4) 100–200 µg/mL (OP5, OP7) 400–800 µg/mL (OP6)	400–800 µg/mL (OP1, OP7) 800–1600 µg/mL (OP3) >1600 µg/mL (OP2, OP4–OP6)	[44]
	≤4.0 mg/mL (acetone extract, ethyl acetate extract), ≤1.0 mg/mL (ethanol extract), ≤2.0 mg/mL (methanol extract), ≤4.0 mg/mL (DMSO extract)		[31]
	1.25%		[36]
	292.97 µg/mL	1171.87 µg/mL	[85]
	6.25–25 µg/mL	50–100 µg/mL	[34]
	7.44 mg/mL	>29.76 mg/mL	[14]
	300 µg/mL		[90]
	0.90 to 8.22 mg/mL		[72]
	15.7 µg/mL (EEP)		[74]
	0.6–1.2 mg/mL	0.6–1.2 mg/mL	[75]
	50 mg/mL (aqueous extract) 100 mg/mL (hydroalcoholic extract)	25 mg/mL (aqueous extract)	[91]
	12.5 µg/mL		[7]
	625 µg/mL		[97]
	250 µg/mL		[92]
	5.0 µg/mL (cold ethanolic propolis and hot ethanolic propolis)		[94]
	2.65 mg/mL		[87]
	240 µg/mL	480 µg/mL	[98]
1.16 µg/mL		[93]	
<i>Streptococcus oralis</i>	12.5–25 µg/mL (OP1–OP3) 25–50 µg/mL (OP4–OP7)	100–200 µg/mL (OP1, OP2, OP7) 200–400 µg/mL (OP3, OP6) 400–800 µg/mL (OP4, OP5)	[44]
	0.3 mg/mL (German ethanol extract) 0.1 mg/mL (Czech ethanol extract, Irish ethanol extract) 1.2 mg/mL (German water extract)	0.6 mg/mL (German ethanol extract) 0.3 mg/mL (Czech ethanol extract, Irish ethanol extract) 5.0 mg/mL (German water extract)	[84]
	25 µg/mL	50 µg/mL	[34]
	125 µg/mL		[92]
<i>Streptococcus parasanguinis</i>	25 µg/mL	200 µg/mL	[34]

Table 3. Cont.

Bacteria	MIC	MBC	Reference
<i>Streptococcus pyogenes</i>		5–10 mg/mL	[60]
	0.6 mg/mL (German ethanol extract, German water extract) 0.08 mg/mL (Czech ethanol extract, Irish ethanol extract)	1.2 mg/mL (German ethanol extract) 0.6 mg/mL (Irish ethanol extract) 0.1 mg/mL (Czech ethanol extract) 2.5 mg/mL (German water extract)	[84]
	156 µg/mL		[89]
	8.0 µg/mL		[76]
	512–1024 µg/mL		[71]
<i>Streptococcus sanguinis</i>	30 µg/mL		[62]
	1.25%		[36]
	7.44 mg/mL	>29.76 mg/mL	[14]
	12.5 µg/mL		[7]
	125 µg/mL		[92]
	60 µg/mL	120 µg/mL	[98]
	1.8 µg/mL		[93]
<i>Streptococcus salivarius</i>		5–20 mg/mL	[60]
	90–100 µg/mL		[62]
	500 µg/mL (ethanol extract)	500 µg/mL (ethanol extract)	[15]
	0.6–1.2 mg/mL	0.6–1.2 mg/mL	[75]
	≤1 mg/mL (ethyl acetate extract), ≤2 mg/mL (acetone extract, methanol extract)		[31]
	0.6–1.2 mg/mL	0.6–1.2 mg/mL	[75]
	3.12–25 µg/mL	50–100 µg/mL	[34]
	7.44 mg/mL	7.44 mg/mL	[14]
1.16 µg/mL		[93]	
<i>Streptococcus sobrinus</i>	25 µg/mL (EEP BA), 50 µg/mL (EEP RS), 400 µg/mL (EEP MG)	100 µg/mL (EEP BA), 200 µg/mL (EEP RS), >800 µg/mL (EEP MG)	[21]
	25–100 µg/mL	200–800 µg/mL	[59]
		5–20 mg/mL	[60]
	2 µg/mL		[61]
	200 µg/mL		[62]
	25–50 µg/mL	200–400 µg/mL	[63]
	<6.25 µg/mL	50–100 µg/mL	[68]
	70 µg/mL		[65]
0.90–8.22 mg/mL		[72]	

Table 3. Cont.

Bacteria	MIC	MBC	Reference
	4.0–8.0 µg/mL	8.0 µg/mL	[77]
<i>Streptococcus sobrinus</i>	25–50 µg/mL (OP2)	>1600 µg/mL (OP1–OP7)	[44]
	50–100 µg/mL (OP1, OP3, OP4)		
	100–200 µg/mL (OP7)		
	400–800 µg/mL (OP5, OP6)		
	1.25%		
	25 µg/mL	100 µg/mL	[34]
	625 µg/mL		[97]
<i>Streptococcus uberis</i>	25 µg/mL	100 µg/mL	[34]
<i>Veillonella parvula</i>	20.8 + 10.1 µg/mL *	32.0 + 18.4 µg/mL *	[19]

* mean + SD

4.2.2. In Vivo Studies

The authors of the review study resolved to comment also on *in vivo* studies, since they believed it was important to highlight the important role of honey in the treatment of oral cavity bacterial infections.

Gebara et al. [32] evaluated the additional effect of subgingival cleaning with the use of propolis extract on deep periodontal pockets following a mechanical therapy. In their research, they used both clinical and microbiological parameters. The *in vivo* study indicated that the total viable counts of anaerobic bacteria decreased, the percentage of sites with low levels increased (< 10 CFU/mL) of *P. gingivalis*, and the number CF sites in group A sites in comparison to group B and C decreased. The study included twenty patients with chronic periodontitis. Irrigation was applied in two groups with the use of: a hydro alcoholic solution of propolis extract twice a week for two weeks (group A); a placebo twice/week for two weeks (group B). One group was not additionally treated (C). Two weeks after clinical data recording, the researchers collected subgingival plaque samples. Scaling and root planing were also performed. After another two weeks, irrigation began (baseline). Microbiological and clinical data were collected at baseline and after 4, 6, and 24 weeks [32].

De Carvalho Duailibe et al. [101] analyzed propolis extract activity against *S. mutans in vivo*. The results showed that the propolis extract has an *in vivo* antimicrobial activity against *S. mutans* and might be used as an alternative solution to prevent dental caries. The results were obtained based on the study of forty-one young volunteers who used a rinse of 3 mL propolis extract solution for seven days. During the trial, three samples were collected (first: in the morning, the second: 1 hour after the first use of the solution, and the third sample was obtained after 7 days). The alterations in the number of colonies of *S. mutans* were observed in patients between the 1st and 2nd collection, i.e., a decrease in 62% of samples, an increase in 14% of samples, and no change in 24% of samples (an important difference in the number of *S. mutans* between the collections 1 and 2 defined as mean ± SD, 4.275 ± 0.8459 versus 2.809 ± 2.0911). Whereas, between the 1st and 3rd collection, the bacterial concentration detected in patients translated into a reduction in 81% of samples, an increase in 9.5% of samples, and no change in 9.5% samples (between collections 1 and 3: 4.275 ± 0.8459 versus 2.4184 ± 1.9999). Consequently, a reduced number of *S. mutans* both after the beginning (collection 2) and after the full treatment (collection 3) was observed [101].

Another group of researchers, Machorowska-Pieniążek et al. [102], assessed the effect of 3% ethanol extract of propolis (EEP) on the microbiological status of the oral cavity in patients with cleft lip and palate, which were treated with fixed orthodontic appliances. The percentage of the *Actinomyces spp.* and *Capnocytophaga spp.* was statistically significantly decreased compared with baseline in the propolis group. However, such a result was

not obtained for *Streptococcus spp.* Forty-one patients participated in the study, and they were divided into two subgroups. The I subgroup included twenty-one patients who used propolis toothpaste to brush their teeth three times a day, while in the II subgroup, there were twenty patients who brushed their teeth three times a day with toothpaste without propolis, and they constituted the control group. The next step involved the collection of the supragingival bacterial plaque from each patient at baseline and after using the toothpaste for 35 days [102].

Skaba et al. [37] tried to answer the question of how toothpaste with Brazilian extract of propolis (EEP) affected oral health. Their results suggested that the microbial action of EEP at 50 mg/L concentration was time-dependent, and EEP revealed antimicrobial activity against *S. intermedius*. The researchers examined oral microflora from thirty-two adult patients with marginal periodontium to obtain their results [37].

Sanghani et al. [27] evaluated whether Indian propolis extract used subgingivally could supplement scaling and root planing (SRP) in the treatment of periodontitis. The obtained results indicated that the groups showed a reduction in the microbial count of *P. gingivalis*, *P. intermedia*, and *F. nucleatum*. The results were obtained based on the study of forty patients diagnosed with chronic periodontitis who were divided into two groups: the I group (twenty patients who received SRP alone) and the II group (twenty patients who received SRP and locally delivered propolis). The samples of subgingival plaque were collected at baseline, after 15 days, and one month, and they were cultured for periodontal pathogens in anaerobic conditions [27].

Kumar et al. [38] evaluated the efficacy of propolis tooth gel on plaque inhibition. The study showed a significant reduction in *P. gingivalis* only in the first group, while all three strains (*P. gingivalis*, *T. forsythia*, and *T. denticola*) were significantly decreased in the propolis group. The results were obtained based on the study of forty patients with chronic periodontitis who were classified into two groups: the I group (twenty patients used *Aloe vera* gel) and the II group (twenty patients used propolis gel for 3 months) [38].

El-Sayed et al. [103] assessed the impact of ethanol propolis extract mouthwash on oral microflora. The study indicated about a 25-fold decrease in the total bacterial count after propolis mouthwash use, but the observed decrease was lower in comparison to chlorhexidine (about an 1107-fold decrease). The results were obtained in the study of ninety children who were classified into two groups: the I group (forty-five children used a propolis extract containing mouthwash for 1 minute three times a day for 5 days), and the II group (forty-five children used 0.2% chlorhexidine containing mouthwash) [103].

Niedzielska et al. [4] analyzed the effect of 3% Brazilian green propolis extract gel on oral microbiota. The authors noticed a time-dependent decrease in the number of oral microorganisms from 28 strains of microorganisms of 54 species at the beginning to 48 microorganisms strains of 20 species after 22 days of treatment in the study group. In contrast, the number of strains in the control group increased from 18 to 25 after 22 days. The comparison of microorganisms between the 1st and 22nd day of treatment showed that eight new strains occurred (*S. oralis*, *S. vestibularis*, *S. aureus* MSSA, *V. parvula*, *B. longum*, *L. acidophilus*, *C. ramosum*, and *F. nucleatum*), while 15 strains were eliminated (*R. productus*, *B. adolescentis*, *B. infantis*, *A. israelii*, *A. naeslundii*, *A. odontolyticus*, *A. viscosus*, *C. perfringens*, *C. spp.*, *B. distasonis*, *C. gracile*, *C. ochracea*, *M. multiacidus*, *P. bivia*, and *P. melaninogenica*). The results were obtained based on the study of thirty-one patients who were classified into two groups: the I group (sixteen patients used propolis gel) and the II group (fifteen patients used a placebo for 1, 8, and 22 days) [4].

Piekarz et al. [23] focused on how toothpaste with Australian *Melaleuca alternifolia* oil and ethanolic extract of Polish propolis affected the microbiome and the hygiene of the oral cavity. The authors observed that in the propolis group, 305 bacterial strains were identified, while 321 strains of bacteria were identified in the *Melaleuca alternifolia* group. In case of the propolis group, the number of strains decreased, while in the control group, they increased. In the propolis group, *S. mitis*, *S. sanguis*, *S. salivarius*, *A. israelii*, *A. naeslundii*, *C. perfringens*, and *L. acidophilus* were decreased, while *C. gracilis* was eradicated. The

results were obtained in the study of fifty-one patients who were classified into two groups: the I group (twenty-five patients used toothpaste with the active ingredients: *Melaleuca alternifolia* oil and 1.5% ethanol extract of Polish propolis), and the II group (twenty-six patients used negative control toothpaste) [23].

Pundir et al. [26] analyzed the impact of one-stage full-mouth disinfection with the use of 20% propolis hydroalcoholic solution. The *in vivo* study group comprised chronic periodontitis patients. The authors noticed the reduction in microbial count for *A. actinomycetemcomitans*, *P. gingivalis*, and *P. intermedia* after 12 weeks of treatment in comparison to control (413.33 ± 103.83 and 554.53 ± 135.37 , 383.07 ± 114.6 and 470.8 ± 87.21 , as well as 347.47 ± 105.94 and 512.73 ± 183.34 , respectively). The results were obtained based on the study of thirty patients who were classified into two groups: the I group (fifteen patients used 20% propolis hydroalcoholic solution for 3 months) and the II group (fifteen patients were a control) [26].

Wiatrak et al. [8] analyzed the effect of a Polish propolis and tee tree oil-containing hygienic agent on certain oral health parameters, oral microflora, and the condition of periodontal health *in vivo*. The authors observed a significant improvement in hygiene and the condition of the periodontium in the propolis group. The microbial investigation showed that in the propolis group in the first test, 77 microorganisms of 31 species were isolated, after 7 days of treatment, 78 microorganisms of 27 species were isolated, while after 4 weeks of treatment, only 65 microorganisms of 24 species were isolated. The bacterial species which were eliminated included: *A. viscosus*, *A. israelii*, *A. parvulum*, *B. ovatus*, *C. botulinum*, *E. saburreum*, *L. acidophilus*, *L. fermentum*, and *P. granulosum*. The microflora gained the following species: *A. minutum*, *C. butyricum*, *C. ochracea*, *P. melaninogenica*, *M. spp.*, *S. oralis*, *P. rustigiani*, and *S. maltophilia*. In the control group in the first test, 79 microorganisms of 25 species were isolated, after 7 days of treatment, 83 microorganisms of 28 species were isolated, while after 4 weeks of treatment, 92 microorganisms of 26 species were isolated. The eradicated bacterial species included: *C. sporogenes*, *E. saburreum*, *L. fermentum*, *B. ovatus*, *B. uniformis*, *F. mortiferum*, *P. oralis*, and *S. aureus*. The microflora gained the following species: *C. chauvoei*, *P. propionicum*, *S. mutans*, and *N. sicca*. The number of the following bacteria declined: *B. producta*, *C. clostridiforme*, *L. acidophilus*, *C. ochracea*, and *S. sanguinis*, but the count of certain bacteria increased: *A. israelii*, *A. naeslundii*, *C. gracilis*, *S. mitis*, *S. salivarium*, and *N. subflava*. The results were obtained in the study of thirty-seven patients who were divided into two groups: the I group (eighteen patients used toothpaste with the active ingredients: tea tree oil and 1.5% ethanol extract of Polish propolis), and the II group (nineteen patients used negative control toothpaste) [8].

Peycheva et al. [16] analyzed the effect of marketed toothpaste and the addition of the extract of Bulgarian propolis to the toothpaste on oral microbial flora. The authors showed that the Bulgarian propolis in the toothpaste may improve the oral hygiene of patients, since it increases oral health, gingival condition, and activity against periodontal and cariogenic pathogens. The authors noticed a decrease in *S. mutans* samples from nine to four and from 10 to zero, respectively for the control and propolis groups. The study showed that the propolis extract completely eradicated *S. mutans*, *F. varium*, Gram-negative cocci, Gram-positive rods, *P. asaccharolyticus*, *P. bivia*, *P. intermedia*, *P. melani*, and *S. intermedius*. *Neisseria spp.* and *S. viridans* were resistant, since both strains were presented before and after treatment. No side effects were noticed by the authors in either group. The results were obtained based on the study of thirty-five students who were classified as follows: the I group (used marketed toothpaste in their routine oral hygiene) and the II group (added 10 drops of Propolin containing standardized 20% hydroalcoholic extract of Bulgarian propolis to the toothpaste before every brushing for 20 days) [16].

El-Allaky et al. [104] assessed the antimicrobial properties of 2% pure propolis in chewing gum and mouthwash against *S. mutans*. The authors observed that propolis in chewing gum and/or mouthwash can be used in the bacterial treatment in high caries risk children. The results were obtained based on the study of sixty children who constituted two study groups: the I group (thirty children received propolis chewing gum), and the II

group (thirty children received propolis mouthwash). In both groups, the authors observed a highly significant difference between the mean values of the absolute total bacterial count before and after the intervention. The percentage changes were 28.95 ± 10.66 and 31.65 ± 14.62 for the groups I and II, respectively. In case of the absolute count of *S. mutans*, no significant differences were observed before and after treatment. The percentage change decreased by 64.85 ± 38.30 and $66.47 \pm 37.84\%$ for the groups I and II, respectively [104].

The antibacterial efficacy of a propolis-based dentifrice was assessed by Mohsin et al. [105], and the study focused on *S. mutans*, which colonized the oral cavity of young patients. The researchers observed an *in vivo* antimicrobial activity of propolis dentifrice against *S. mutans*. The study was carried out on 30 children who used propolis dentifrice (Probee,™ Quasi-Medical Products, Seoul Propolis) daily for three minutes over four weeks. The samples of plaque and saliva were collected at baseline as well as in the 1st week, 3rd week, and 4th week, and *S. mutans* count was estimated with the use of a Dentocult®SM strip Mutans kit (Orion Diagnostica Oy, Finland). The mean *S. mutans* count during the 1st week and 4th week was significantly reduced when compared to baseline scores. The researchers recorded a statistically significant difference between the baseline count and the 1st week, 3rd week and 4th week follow up [106]. Alkhaled et al. (2021) examined the *in vivo* effect of chlorhexidine and propolis on *S. mutans*. The authors observed a decrease in the number of *S. mutans* strains before and after treatment and showed that propolis was almost as effective in its antimicrobial activity as chlorhexidine. The results were obtained based on the study of forty children classified into two study groups: the I group (twenty children used mouthwash with 0.12% chlorhexidine) and the II group (twenty children used mouthwash with 5% propolis). Children were not allowed to use any oral rinse or toothpaste with chlorhexidine 7 days before any clinical procedures began. During the study, two samples were collected: 1st at the beginning and 2nd after the child rinsed their mouth with 10 mL of solution for 30 seconds. Then, colonies were counted from both obtained samples (CFU/mL). In the first group, the observed decrease was from 173.70 to 25.2, while in the II group, it was from 158.45 to 15.90. In addition, the following results were obtained: a decrease in the number of *S. mutans* calculated between two sample collections expressed as percentage, for three experimental groups. The propolis group and chlorhexidine group reduction ratios were 85.49% and 89.97%, respectively [105].

Bapat et al. [94] evaluated the efficiency of propolis mouth rinses on oral pathogens. The authors determined propolis as an effective agent against oral pathogens *S. mutans* and *L. acidophilus*. The results were obtained in the study of one hundred and twenty patients who were classified into four groups: the I group (used hot ethanolic propolis extract), the II group (used cold ethanolic propolis extract), the III group (used chlorhexidine), and the IV group (used distilled water—placebo). There was a washout period of two weeks, and oral prophylaxis and polishing were performed. Subjects rinsed their oral cavities twice a day for 3 months. Saliva was collected at baseline, after 5 minutes, and after 1 h for a microbiological analysis. The colony count was performed using an electron microscope for *L. acidophilus* and *S. mutans* and was expressed as the number of CFU per mL of saliva. There were six concentrations of propolis in each group (2 µg/mL; 5 µg/mL; 10 µg/mL; 25 µg/mL; 50 µg/mL and 75 µg/mL). For *S. mutans*, hot ethanol propolis mouthwashes obtained the following results: 2 µg/mL (resistant); 5 µg/mL (8.25 ± 1.20); 10 µg/mL (11.12 ± 1.20); 25 µg/mL (12.05 ± 1.01); 50 µg/mL (12.08 ± 0.707) and 75 µg/mL (12.80 ± 2.558). *S. mutans* for cold ethanol propolis mouthwashes obtained the following results: 2 µg/mL (resistant); 5 µg/mL (7.78 ± 1.15); 10 µg/mL (8.50 ± 0.56); 25 µg/mL (13.56 ± 1.20); 50 µg/mL (14.40 ± 0.894) and 75 µg/mL (15.60 ± 1.949). For *L. acidophilus*, hot ethanol propolis mouthwashes obtained the following results: 2 µg/mL (resistant); 5 µg/mL (8.25 ± 1.25); 10 µg/mL (8.05 ± 1.16); 25 µg/mL (13.60 ± 1.14); 50 µg/mL (17.70 ± 0.447) and 75 µg/mL (19.80 ± 0.901). For *L. acidophilus*, cold ethanol propolis mouthwashes obtained the following results: 2 µg/mL (resistant); 5 µg/mL (7.25 ± 1.77);

10 µg/mL (8.45 ± 2.20); 25 µg/mL (10.55 ± 1.23); 50 µg/mL (15.20 ± 1.789) and 75 µg/mL (17.60 ± 3.130) [94].

Faveri et al. [25] analyzed the impact of 3% Brazilian propolis extract and 0.12% chlorhexidine on 39 bacterial species of oral microbiota. The authors suggest that the use of a 3% propolis mouth rinse can prevent morning breath. The results were obtained based on the study of thirty patients who were classified into three groups: the I group (ten patients used placebo), the II group (10 patients used 3% Brazilian propolis ethanol extract), and the III group (ten patients used 0.12% chlorhexidine). At the day 10 time point, no significant differences were observed. Between the 10 and 15 time points, a significant reduction in *P. nigrescens*, *A. naeslundii*, *F. periodonticum*, *P. intermedia*, *P. gingivalis*, *T. denticola*, *C. ocheacea*, *A. naeslundii*, *A. isrelli*, and *T. forsythia* in the II group was observed. *P. acnes* showed a significant increase in the II group. In the III group, the authors observed a significant reduction in *T. forsythia*, *P. gingivalis*, and *T. denticola*. In case of the I group, a significant increase in *A. naeslundii*, *P. micra*, *S. oralis*, *F. nucleatum ssp vincentii*, *P. acnes*, *E. nodatum*, and *S. anginosus* was observed after 5 days of treatment. The total counts of organisms present on the tongue surface showed a significant decrease for the II and III groups [25].

Patients who had periodontal disease constituted the group studied by Lisbona-González et al. [29]. The researchers evaluated the antimicrobial effects of a mouthwash with propolis and assessed how the propolis paste formulation affected dental healing after teeth extraction. The common staining of the mouth/tongue could be avoided when propolis and chlorhexidine were used as ingredients of the mouthwash. Moreover, propolis paste proved to be an alternative substance to be used after dental extraction for healing the socket. Additionally, this paste could control the inflammatory process more effectively over the experimental period. A decrease in CFU of *S. mutans* and *Lactobacillus spp.* observed in propolis and chlorhexidine + propolis samples was recorded by researchers [29].

In another study, Lisbona-González et al. [42] evaluated how Spanish propolis extract (EEP) affected the clinical and microbiological parameters when it was used as an adjuvant to scaling and root planning in supportive periodontal therapy (SPT) patients. The authors suggest that EEP used subgingivally could be a helpful adjuvant in periodontal therapy, since microbial resistance and other adverse effects could be eliminated. The results were obtained based on the study of forty patients who were classified into three groups: the I group (twenty patients who underwent scaling and root planning, after which physiological saline was used for gingival irrigation—the controls) and the II group (twenty patients who underwent scaling and root planning after which EEP was placed subgingivally). The researchers concluded that EEP could be used in prophylaxis and in the treatment of periodontal diseases. EEP would improve clinical parameters, reduce gingival bleeding, and decrease the number of *T. forsythensis* and *P. gingivalis* [42].

Lotif et al. [107] researched the antimicrobial effect of Brazilian red propolis on *Lactobacillus spp.* The authors showed that Brazilian red propolis has antibacterial activity against the analyzed strains. The results were obtained based on the study of forty-two participants who were divided into three groups: the I group (fluoridated Brazilian red propolis dentifrice) and the II group (fluoridated common dentifrice). For the first dilution (1:10), the analysis of *Lactobacillus spp.* strains from patients' saliva showed a decrease in the count of the analyzed strain from 1.15 ± 0.41 at day 0 to 0.68 ± 0.15 on day 28 for the I group as well as an increase from 1.33 ± 0.52 on day 0 to 1.84 ± 0.39 at day 28 for the II group. For the second dilution (1:100), the corresponding values in G1 and G2 were 0.87 ± 0.34 and 0.64 ± 0.37 as well as 1.54 ± 0.47 and 1.62 ± 0.37 , respectively [107].

Naggar et al. [108] selected a group of high caries risk patients for their study to research propolis and pomegranate mouthwashes in comparison with chlorhexidine mouthwash. The aim of the study was to assess their antibacterial activity. The researchers found out that propolis and pomegranate mouthwashes could constitute an alternative to chlorhexidine mouthwash. The results were obtained based on the study of eighty patients who were divided into four groups: the I group (used propolis mouthwash), the II group (used pomegranate mouthwash), the III group (used chlorhexidine mouthwash), and the

IV group (used saline). The sample of saliva was collected at baseline, immediately after the application of mouthwash, and after seven days. pH values of the saliva samples and *S. mutans* bacterial count were estimated. No statistically significant difference between the total percentage reduction in bacterial counts was observed in all groups. However, the lowest values were recorded immediately after the use [108].

Nakao et al. [109] studied the effect of topical application of an oral gel containing propolis on radiotherapy-related oral complications caused by *P. gingivalis*. The authors confirmed that propolis is not only effective in decreasing the number of *P. gingivalis* but also relieves oral pain. The results were obtained based on the study of twenty-seven patients who were divided into five groups: the I group (six patients used an oral gel with placebo), the II group (five patients used an oral gel with chlorhexidine), the III group (five patients used an oral gel with curry leaf), the IV group (six patients used an oral gel with propolis), and the V group (five patients used an oral gel with turmeric). The participants of the study were informed about the procedures during the first visit and gave their consent. Then, samples were collected before and after the treatment, during the second and fourth visit. Each subject used gel once every night after brushing their teeth for 1 month during the study. They were asked to collect saliva themselves before brushing their teeth in the morning during the second and fourth visit. Propolis was used at the concentration of 100 µg/mL and inhibited both the growth and biofilm formation of *P. gingivalis*. At the baseline visit, 92% of subjects felt dryness in the oral cavity, and 52% of subjects had pain in the oral cavity. Each intervention was examined on bacteria clearance in saliva by species-specific real-time PCR analysis. For propolis, the amount of *P. gingivalis* in saliva was reduced from 100 to 20% [109].

Siqueira et al. [110] analyzed *in vivo* the effects of Brazilian red propolis and xylitol chewable tablets. The obtained results suggest that the tablets can be not only an effective alternative, but they cost less. Moreover, they are natural adjuncts which could be applied to prevent dental caries and other periodontal diseases. The results were obtained based on the study of twelve participants who were divided into three groups: the I group (used placebo) and the II group (used the tested tablets). The analysis of saliva showed a decrease in the CFU of *S. mutans*. The log₁₀CFU/mL values were 2.74 and 2.52, respectively, for before and after treatment for the II group. For the placebo group, the log₁₀CFU/mL values were 2.20 and 2.29, respectively, for before and after treatment [110].

Wiatrak et al. [111] evaluated tea tree essential oil (TTO) toothpaste with natural and ethanolic extract of propolis (EEP). They focused on the effect on microflora and certain oral health indicators. The study group included the patients who used removable acrylic partial dentures. The study proved that toothpaste with natural antimicrobial substances significantly decreased the number of oral microbiota. Therefore, the antimicrobial and antifungal activity of those natural antimicrobial substances, i.e., TTO and EEP, was confirmed. The results were obtained based on the study of fifty patients who were divided into three groups: the I group (which used the toothpaste with TTO and EEP) and the II group (which used the same toothpaste but without TTO and EEP). Control visits took place 7 and 28 days later and were compared to baseline. The authors observed a decrease in the number of strains isolated from smears from 108 microorganisms (1st day) to 96 strains (7th day) and 80 strains (28th day) in the group using toothpaste. In the control group, the number of microorganisms increased from 100 strains (1st day) to 101 (7th day) and 104 (28th day) [111].

Seth et al. [112] evaluated the antimicrobial activity of 25% propolis extract irrigation. The obtained results suggest that the propolis extract is as effective as chlorhexidine. Moreover, the propolis extract plays an important role in periodontal therapy. The results were obtained based on the study of twenty patients who were divided into three groups: the I group (received irrigation with 0.2% chlorhexidine) and the II group (received irrigation with 25% propolis extract). The obtained results of CFU indicated a reduction in the number of the colony from 1500 ± 135.54 to 75 ± 14.28 for the I group and from 1445 ± 137.21 to 82.5 ± 13.59 from the II group [112].

5. Discussion

Taking into account the MIC and MBC values as well as the inhibition zones for different microorganisms, which could be found in the reviewed papers, we prepared Figure 3a–c, which shows mean values of MIC and MBC in $\mu\text{g/mL}$ as well as inhibition zone in mm.

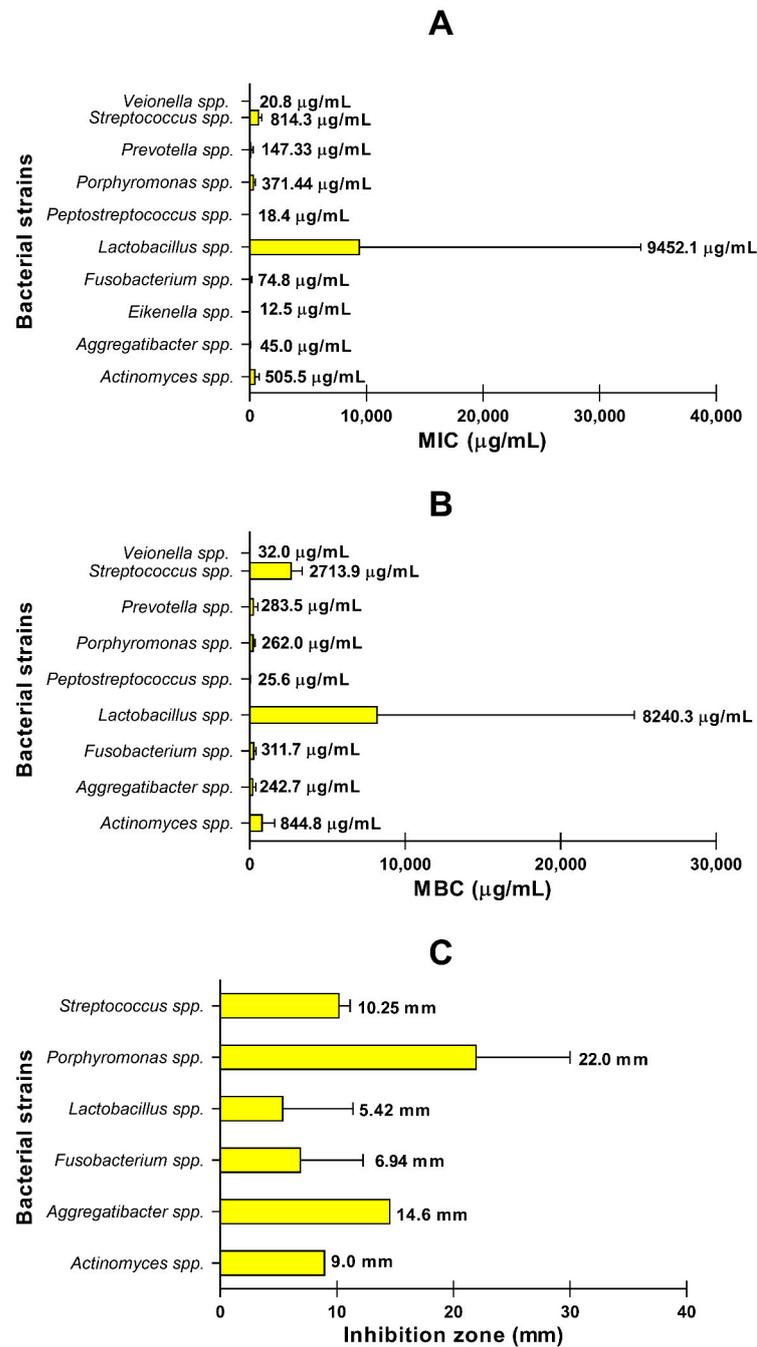


Figure 3. Antibacterial activity of propolis: (a) The mean MIC values \pm SEM expressed in $\mu\text{g/mL}$ for the bacterial strains causing oral cavity infections [7,14,15,19,21,34,36,59–65,68,71,72,75–77,82,84,85, 87,89–94,97,98,100]; (b) The mean MBC values \pm SEM expressed in $\mu\text{g/mL}$ for the bacterial strains causing oral cavity infections [14,15,19,21,34,59,60,63,66,68,75,77,82,84,85,91,98,100]; (c) The mean inhibition zone \pm SEM expressed in mm for the bacterial strains causing oral cavity infections [6,15, 31,63,64,66,67,73,81,83,86,93,95,96].

Based on the average values of MIC ($\mu\text{g}/\text{mL}$) (Figure 3a), it can be concluded that the lowest MIC values for propolis were recorded in *Eikenella spp.*, *Peptostreptococcus spp.*, and *Veionella spp.* Propolis exhibited the highest antimicrobial activity against the same strains. Interestingly, various types of propolis did not affect *Actinomyces spp.*, *Lactobacillus spp.*, and *Streptococcus spp.* (average MIC: 0.50, 9.45, and 0.81 mg/mL, respectively). For MBC (in $\mu\text{g}/\text{mL}$) (Figure 3b), the highest antimicrobial activity was recorded in case of *Peptostreptococcus spp.*, and *Veionella spp.* It is noteworthy that *Actinomyces spp.*, *Lactobacillus spp.*, and *Streptococcus spp.* (average MBC: 0.84, 8.24, and 2.71 mg/mL, respectively) were also the most resistant to different types of propolis. In case of the inhibition zone (Figure 3c), the most sensitive to propolis extract are *Porphyromonas spp.*, *Aggregatibacter spp.*, *Streptococcus spp.*, *Actinomyces spp.*, and *Fusobacterium spp.* with inhibition zones of 2.20, 1.46, 1.02, 0.90, and 0.69 cm, respectively. The most resistant is *Lactobacillus spp.* with an inhibition zone of 0.54 cm. Moreover, the presented results confirm that propolis may be employed to treat bacterial infections of the oral cavity, such as periodontitis, tooth decay, supragingival plaque, subgingival plaque, gingivitis, RAS, and pharyngitis.

The observed high values of SEM In MIC and MBC recorded for the same genus of bacteria may result from the fact that the bee product effect persists over varied amounts of time in the tested microorganisms. Moreover, propolis may contain various active substances at different concentrations. The sensitivity of the tested bacterial strains differed, and researchers used various methods to estimate their bioactivity [113]. To achieve the standardization of bee products, a lot of aspects must be taken into consideration [114]:

- Composition: depends on the geographic specificity of the region, ecoregions, flora, and on when and how bee products were collected;
- The content of the nutritional and active ingredients;
- The storage condition: raw propolis at 4°C or -20°C in dark for 30 days;
- Different assessment methods, e.g., GC-MS to analyze the chemical composition of raw propolis, HPLC in gradient mode coupled with PAD to analyze the most appropriate ingredients of propolis, headspace solid-phase microextraction (HS-SPME) techniques to establish the fingerprint of raw propolis samples from various regions, and electrochemical techniques to determine the antioxidant properties of propolis samples at an early stage.

The review by Luo et al. [114] discusses thoroughly the above-listed issues.

6. Conclusions

Propolis is a natural bee product containing even over 300 different active substances such as resin and balsams, essential oils and wax, pollens, amino acids, enzymes, minerals, vitamins, glucose, flavonoids, phenolic compounds, aromatic acids, esters, terpenes, and beta-steroids. A lot of the mentioned substances possess antibacterial activity—especially flavonoids, which increase bacterial membrane permeability as well as inhibit bacterial genetic coding, nucleic acid synthesis, the attachment and formation of biofilms, the energy metabolism of bacteria, or bacterial nucleic acid synthesis. Caffeic acid phenethyl ester also increases bacterial membrane permeability and inhibits bacterial RNA polymerase. It should be highlighted that the geographic zone of origin, specificity of local flora, plant sources, and the collection season are responsible for the diversity of biologically active compounds present in bee products.

Our review, based on *in vitro* and *in vivo* studies, shows that propolis is a very promising product for treating bacterial infections of the oral cavity, which can lead to periodontitis, gingivitis, caries, plaque (supragingival and subgingival), recurrent aphthous ulcers (RAS), and pharyngitis. Moreover, propolis in comparison to the pharmacological treatment of bacterial infections is much safer, since it does not lead to as many side effects as antibiotic treatment. Hypersensitivity represents a more frequent side effect of propolis, which results in allergic reactions. Taking into account the observed results as well as the biologically active compounds of propolis, more research is needed to determine its chemical composition and to describe the side effects of various types of propolis to select a safe concentration.

Propolis appears to be an adequate alternative to the medications used daily to treat oral bacterial infections.

Author Contributions: The literature search and selection process, data extraction, data analysis, results interpretation, writing—original draft preparation, M.O.; data extraction, data analysis, results interpretation, writing—original draft preparation, L.M.; data analysis, results interpretation, writing—original draft preparation, N.T.; writing—original draft preparation, J.S.; writing—original draft preparation A.R.-S.; writing—review and editing, A.K.-G.; writing—review and editing, M.G.; writing—review and editing, P.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Medical University of Silesia in Katowice, Poland, grant number PCN-1-065/K/1/F.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

- Wayzata Dental. Available online: <https://www.wayzatadental.com/dental-statistics> (accessed on 10 March 2022).
- Oral Health Statistics in the UK. Available online: <https://www.dentalhealth.org/oral-health-statistics> (accessed on 10 March 2022).
- Delivering Better Oral Health: An Evidence-Based Toolkit for Prevention. Available online: <https://www.gov.uk/government/publications/delivering-better-oral-health-an-evidence-based-toolkit-for-prevention/chapter-5-periodontal-diseases> (accessed on 10 March 2022).
- Niedzielska, I.; Puszczewicz, Z.; Mertas, A.; Niedzielski, D.; Rózanowski, B.; Baron, S.; Konopka, T.; Machorowska-Pieniążek, A.; Skucha-Nowak, M.; Tanasiewicz, M.; et al. The influence of ethanolic extract of Brazilian green propolis gel on hygiene and oral microbiota in patients after mandible fractures. *BioMed. Res. Int.* **2016**, *2016*, 9190814. [[CrossRef](#)] [[PubMed](#)]
- Brailsford, S.R.; Tregaskis, R.B.; Leftwich, H.S.; Beighton, D. The predominant *Actinomyces spp.* isolated from infected dentin of active root caries lesions. *J. Dent. Res.* **1999**, *78*, 1525–1534. [[CrossRef](#)] [[PubMed](#)]
- Koo, H.; Gomes, B.P.; Rosalen, P.L.; Ambrosano, G.M.; Park, Y.K.; Cury, J.A. In vitro antimicrobial activity of propolis and *Arnica montana* against oral pathogens. *Arch. Oral Biol.* **2000**, *45*, 141–148. [[CrossRef](#)]
- Tambur, Z.; Miljković-Selimović, B.; Opačić, D.; Vuković, B.; Malešević, A.; Ivančajić, L.; Aleksić, E. Inhibitory effects of propolis and essential oils on oral bacteria. *J. Infect. Dev. Ctries.* **2021**, *15*, 1027–1031. [[CrossRef](#)] [[PubMed](#)]
- Wiatrak, K.; Morawiec, T.; Rój, R.; Mertas, A.; Machorowska-Pieniążek, A.; Kownacki, P.; Tanasiewicz, M.; Skucha-Nowak, M.; Baron, S.; Piekarczyk, T.; et al. Oral health of patients treated with acrylic partial dentures using a toothpaste containing bee product. *Evid.-Based Complement. Altern. Med.* **2017**, *2017*, 4034179. [[CrossRef](#)] [[PubMed](#)]
- Dina, M.N.; Märgärit, R.; Andrei, O.C. Pontic morphology as local risk factor in root decay and periodontal disease. *Room J. Morphol. Embryol.* **2013**, *54*, 361–364.
- Jabuk, S.I.; Rafla'a, S.H.; Hussein, Z.M.A.; Najam, H.M.; Naji, N.M. Isolation and identification of bacteria and parasite from teeth caries and periodontal. *Adv. Environ. Biol* **2015**, *9*, 50–53.
- Mantzourani, M.; Fenlion, M.; Beighton, D. Association between *Bifidobacteriaceae* and the clinical severity of root caries lesions. *Oral Microbiol. Immunol.* **2009**, *24*, 32–37. [[CrossRef](#)]
- Panesar, P.S.; Kumari, S. Lactulose: Production, purification and potential applications. *Biotech. Adv.* **2011**, *29*, 940–948. [[CrossRef](#)] [[PubMed](#)]
- Yap, D.Y.; To, K.K.; Yip, T.P.; Lui, S.L.; Chan, T.M.; Lai, K.N.; Lo, W.K. *Streptococcus bovis* periodontitis complicating peritoneal dialysis- a review of 10 years' experience. *Perit. Dial. Int.* **2012**, *32*, 55–59. [[CrossRef](#)] [[PubMed](#)]
- Martins, M.L.; Monteiro, A.S.N.; Guimarães, J.E.C.; Guimarães, M.B.D.C.T.; da Silva, R.F.; Cabral, L.M.; Farah, A.; Depaula, J.; Romanos, M.T.V.; Maia, L.C.; et al. Cytotoxic and antibacterial effect of a red propolis mouthwash, with or without fluoride, on the growth of a cariogenic biofilm. *Arch. Oral Biol.* **2019**, *107*, 104512. [[CrossRef](#)] [[PubMed](#)]
- Kashi, T.S.J.; Kermanshahi, R.K.; Erfan, M.; Dashtjerdi, E.V.; Rezaei, Y.; Tabatabaei, F.S. Evaluating the in-vitro antibacterial effect of Iranian propolis on oral microorganisms. *Iran. J. Pharm. Res.* **2011**, *10*, 363–368.
- Peycheva, S.; Apostolova, E.; Gardjeva, P.; Peychev, Z.; Kokova, V.; Angelov, A.; Slavov, A.; Murdjeva, M. Effect of Bulgarian propolis on the oral microflora in adolescents with plaque-induced gingivitis. *Rev. Bras. Farm.* **2019**, *29*, 271–277. [[CrossRef](#)]
- He, P.; Francois, K.; Missaghian, N.; Le, A.D.; Flynn, T.R.; Shanti, R.M. Are bacteria just bystanders in the pathogenesis of inflammatory jaw conditions? *J. Oral Maxillofac. Surg.* **2022**, *80*, 1094–1102. [[CrossRef](#)] [[PubMed](#)]

18. Martin, F.E.; Nadkarni, M.A.; Jaques, N.A.; Hunter, N. Quantitative microbiological study of human carious dentine by culture and real-time PCR: Association of anaerobes with histopathological changes in chronic pulpitis. *J. Clin. Microbiol.* **2002**, *40*, 1698–1704. [[CrossRef](#)]
19. Koru, O.; Toksoy, F.; Acikel, C.H.; Tunca, Y.M.; Baysallar, M.; Uskudar Guclu, A.; Akca, E.; Tuylu, A.O.; Sorkun, K.; Tanyuksel, M.; et al. In vitro antimicrobial activity of propolis samples from different geographical origins against certain oral pathogens. *Anaerobe* **2007**, *13*, 140–145. [[CrossRef](#)]
20. Kouidhi, B.; Zmantar, T.; Hentati, H.; Bakhrouf, A. Cell surface hydrophobicity, biofilm formation, adhesives properties and molecular detection of adhesins genes in *Staphylococcus aureus* associated to dental caries. *Microb. Pathog.* **2010**, *49*, 14–22. [[CrossRef](#)]
21. Koo, H.; Rosalen, P.L.; Cury, J.A.; Ambrosano, G.M.; Murata, R.M.; Yatsuda, R.; Ikegaki, M.; Alencar, S.M.; Park, Y.K. Effect of a new variety of *Apis mellifera* propolis on *mutans Streptococci*. *Curr. Microbiol.* **2000**, *41*, 192–196. [[CrossRef](#)]
22. Refoua, Y. A study of *Streptococcus viridans* in the maxillofacial region. *Front. Dent.* **2005**, *2*, 174–177.
23. Piekarz, T.; Mertas, A.; Wiatrak, K.; Rój, R.; Kownacki, P.; Śmieszek-Wilczewska, J.; Kopczyńska, E.; Wrzoł, M.; Cisowska, M.; Szliszka, E.; et al. The influence of toothpaste containing Australian *Melaleuca alternifolia* oil and ethanolic extract of polish propolis on oral hygiene and microbiome in patients requiring conservative procedures. *Molecules* **2017**, *22*, 1957. [[CrossRef](#)]
24. Moore, W.E.; Holdeman, L.V.; Smibert, R.M.; Good, I.J.; Burmeiser, J.A.; Palcanis, K.G.; Ranney, R.R. Bacteriology of experimental gingivitis in young adult humans. *Infect. Immun.* **1982**, *38*, 651–667. [[CrossRef](#)] [[PubMed](#)]
25. De Faveri, M.; Pupio, G.C.; Koo, H.; Bueno-Silva, B.; de Oliveira, K.M.; Figueiredo, L.C.; Rosalen, P.L.; Hayacibara, R.M.; Fujimaki, M. The effect of Brazilian propolis type-3 against oral microbiota and volatile sulfur compounds in subjects with morning breath malodor. *Clin. Oral Investig.* **2021**, *26*, 1531–1541. [[CrossRef](#)] [[PubMed](#)]
26. Pundir, A.J.; Vishwanath, A.; Pundir, S.; Swati, M.; Banchhor, S.; Jabee, S. One-stage full mouth disinfection using 20% propolis hydroalcoholic solution: A clinico-microbiologic study. *Contemp. Clin. Dent.* **2017**, *8*, 416–420. [[CrossRef](#)] [[PubMed](#)]
27. Sanghani, N.N.; Shivaprasad, B.M.; Savita, S. Health from the hive: Propolis as an adjuvant in the treatment of chronic periodontitis—A clinicomicrobiologic study. *J. Clin. Diagn. Res.* **2014**, *8*, ZC41–ZC44. [[CrossRef](#)] [[PubMed](#)]
28. Patel, M.; Coogan, M.; Galpin, J.S. Periodontal pathogens in subgingival plaque of HIV-positive subjects with chronic periodontitis. *Oral Microbiol. Immunol.* **2003**, *18*, 199–201. [[CrossRef](#)] [[PubMed](#)]
29. Lisbona-González, M.J.; Muñoz-Soto, E.; Lisbona-González, C.; Vallecillo-Rivas, M.; Diaz-Castro, J.; Moreno-Fernandez, J. Effect of propolis paste and mouthwash formulation on healing after teeth extraction in periodontal disease. *Plants* **2021**, *10*, 1603. [[CrossRef](#)] [[PubMed](#)]
30. Brito, F.; Zaltman, C.; Carvalho, A.T.P.; Fischer, R.G.; Persson, R.; Gustafsson, A.; Figueredo, C.M.S. Subgingival microflora in inflammatory bowel disease patients with untreated periodontitis. *Eur. J. Gastroenterol. Hepatol.* **2013**, *25*, 239–245. [[CrossRef](#)] [[PubMed](#)]
31. Mohammad, H.H. In vitro antibacterial activity of propolis alum, miswak, green and black tea, cloves extracts against *Porphyromonas gingivalis* isolated from periodontitis patients in Hilla City, Iraq. *Am. J. Phytomed. Clin. Ther.* **2013**, *1*, 140–148.
32. Gebara, E.C.; Pustigliani, A.N.; de Lima, L.A.; Mayer, M.P. Propolis extract as an adjuvant to periodontal treatment. *Oral Health Prev. Dent.* **2003**, *1*, 29–35.
33. Fosse, T.; Madinier, I.; Hitzig, C.; Charbit, Y. Prevalence of beta-lactamase-producing strains among 149 anaerobic gram-negative rods isolated from periodontal pockets. *Oral Microbiol. Immunol.* **1999**, *14*, 352–357. [[CrossRef](#)]
34. Asgharpour, F.; Moghadamnia, A.A.; Zabihi, E.; Kazemi, S.; Namvar, A.E.; Gholinia, H.; Motallebnejad, M.; Nouri, H.R. Iranian propolis efficiently inhibits growth of oral streptococci and cancer cell lines. *BMC Complement. Altern. Med.* **2019**, *19*, 1–8. [[CrossRef](#)] [[PubMed](#)]
35. Colombo, A.V.; Silva, C.M.; Haffajee, A.; Colombo, A.P.V. Identification of oral bacteria associated with crevicular epithelial cells from chronic periodontitis lesions. *J. Med. Microbiol.* **2006**, *55*, 609–615. [[CrossRef](#)] [[PubMed](#)]
36. Habluetzel, A.; Schmid, C.; Carvalho, T.S.; Lussi, A.; Eick, S. Impact of honey on dental erosion and adhesion of early bacterial colonizers. *Sci. Rep.* **2018**, *8*, 10936. [[CrossRef](#)]
37. Skaba, D.; Morawiec, T.; Tanasiewicz, M.; Mertas, A.; Bobela, E.; Szliszka, E.; Skucha-Nowak, M.; Dawiec, M.; Yamamoto, R.; Ishiai, S.; et al. Influence of the toothpaste with Brazilian ethanol extract propolis on the oral cavity health. *Evid.-Based Complement. Altern. Med.* **2013**, *2013*, 215391. [[CrossRef](#)]
38. Kumar, A.; Sunkara, M.S.; Pantareddy, I.; Sudhakar, S. Comparison of plaque inhibiting efficacies of *Aloe vera* and propolis tooth gels: A randomized PCR study. *J. Clin. Diagn. Res.* **2015**, *9*, ZC01–ZC03. [[CrossRef](#)] [[PubMed](#)]
39. Mashima, I.; Fujita, M.; Nakatsuka, Y.; Kado, T.; Furuichi, Y.; Heratuti, S.; Nakazawa, F. The distribution and frequency of oral *Veillonella spp.* associated with chronic periodontitis. *Medicine* **2015**, *4*, 150–160. [[CrossRef](#)]
40. Sykes, E.A.; Wu, V.; Beyea, M.M.; Simpson, M.T.W.; Beyea, J.A. Pharyngitis: Approach to diagnosis and treatment. *Can. Fam. Physician* **2020**, *66*, 251–257. [[PubMed](#)]
41. Sakamoto, M.; Umeda, M.; Ishikawa, I.; Benno, Y. *Prevotella multififormis* sp. nov., isolated from human subgingival plaque. *Int. J. Syst. Evol. Microbiol.* **2005**, *55*, 815–819. [[CrossRef](#)] [[PubMed](#)]
42. Lisbona-González, M.J.; Muñoz-Soto, E.; Reyes-Botella, C.; Olmedo-Gaya, M.V.; Diaz-Castro, J.; Moreno-Fernandez, J. Study of the antimicrobial effect of an ethanolic extract of propolis in periodontal disease. *Appl. Sci.* **2021**, *11*, 7463. [[CrossRef](#)]

43. Vanni, R.; Waldner-Tomic, N.M.; Belibasakis, G.N.; Attin, T.; Schmidlin, P.R.; Thurnheer, T. Antibacterial efficacy of a propolis toothpaste and mouthrinse against a supragingival multispecies biofilm. *Oral Health Prev. Dent.* **2015**, *13*, 531–535. [[CrossRef](#)] [[PubMed](#)]
44. Reyes, C.P.A.; Dalmacio, L.M.M. Bacterial diversity in the saliva and plaque of caries-free and caries-active Filipino adults. *Med. Biol.* **2011**, *141*, 217–227.
45. Otręba, M.; Marek, Ł.; Tyczyńska, N.; Stojko, J.; Rzepecka-Stojko, A. Bee venom, honey, and royal jelly in the treatment of bacterial infections of the oral cavity: A review. *Life* **2021**, *11*, 1311. [[CrossRef](#)]
46. Ravalia, M.; Wander, P. Bees and dentistry: Are the two linked? *BDJ Pr.* **2020**, *33*, 26–28. [[CrossRef](#)]
47. Abdelrazeg, S.; Hussin, H.; Salih, M.; Shaharuddin, B. Propolis composition and applications in medicine and health. *Int. Med. J.* **2020**, *25*, 1505–1542.
48. Szabat, P.; Poleszak, J.; Szabat, M.; Boreński, G.; Wójcik, M.; Milanowska, J. Apitherapy—the medical use of bee products. *J. Educ. Health Sport* **2019**, *9*, 384–396. [[CrossRef](#)]
49. Przybyłek, I.; Karpiński, T.M. Antibacterial properties of propolis. *Molecules* **2019**, *24*, 2047. [[CrossRef](#)]
50. Hassan, G.; Ghafoor, S. Herbal Medicines: An adjunct to current treatment modalities for periodontal diseases. *Biomedica* **2020**, *36*, 15–22. [[CrossRef](#)]
51. Alvarenga, L.; Cardozo, L.; Borges, N.A.; Chermut, T.R.; Ribeiro, M.; Leite, M., Jr.; Shiels, P.G.; Stenvinkel, P.; Mafra, D. To bee or not to bee? The bee extract propolis as a bioactive compound in the burden of lifestyle diseases. *Nutrition* **2021**, *83*, 111094. [[CrossRef](#)] [[PubMed](#)]
52. Braakhuis, A. Evidence on the health benefits of supplemental propolis. *Nutrients* **2019**, *11*, 2705. [[CrossRef](#)] [[PubMed](#)]
53. Silva, M.V.D.; Moura, N.G.D., Jr.; Motoyama, A.B.; Ferreira, V.M. A review of the potential therapeutic and cosmetic use of propolis in topical formulations. *J. Appl. Pharm. Sci.* **2020**, *10*, 131–141. [[CrossRef](#)]
54. Biharee, A.; Sharma, A.; Kumar, A.; Jaitak, V. Antimicrobial flavonoids as a potential substitute for overcoming antimicrobial resistance. *Fitoterapia* **2020**, *146*, 104720. [[CrossRef](#)] [[PubMed](#)]
55. Almuhayawi, M.S. Propolis as a novel antibacterial agent. *Saudi J. Biol. Sci.* **2020**, *27*, 3079–3086. [[CrossRef](#)] [[PubMed](#)]
56. Andre, C.B.; Chan, D.C.; Giannini, M. Antibacterial-containing dental adhesives' effects on oral pathogens and on *Streptococcus mutans* biofilm: Current perspectives. *Am. J. Dent.* **2018**, *31*, 37B–41B. [[PubMed](#)]
57. Xie, Y.; Yang, W.; Tang, F.; Chen, X.; Ren, L. Antibacterial activities of flavonoids: Structure-activity relationship and mechanism. *Curr. Med. Chem.* **2015**, *22*, 132–149. [[CrossRef](#)] [[PubMed](#)]
58. Cornara, L.; Biagi, M.; Xiao, J.; Burlando, B. Therapeutic properties of bioactive compounds from different honeybee products. *Front. Pharm.* **2017**, *8*, 412. [[CrossRef](#)] [[PubMed](#)]
59. Duarte, S.; Koo, H.; Bowen, W.H.; Hayacibara, M.F.; Cury, J.A.; Ikegaki, M.; Rosalen, P.L. Effect of a novel type of propolis and its chemical fractions on glucosyltransferases and on growth and adherence of *mutans Streptococci*. *Biol. Pharm. Bull.* **2003**, *26*, 527–531. [[CrossRef](#)]
60. Sawaya, A.C.H.F.; Souza, K.S.; Marcucci, M.C.; Cunha, I.B.S.; Shimizu, M.T. Analysis of the composition of Brazilian propolis extracts by chromatography and evaluation of their in vitro activity against gram-positive bacteria. *Braz. J. Microbiol.* **2004**, *35*, 104–109. [[CrossRef](#)]
61. Uzel, A.; Sorkun, K.; Onçağ, O.; Cogulu, D.; Gençay, O.; Salih, B. Chemical compositions and antimicrobial activities of four different Anatolian propolis samples. *Microbiol. Res.* **2005**, *160*, 189–195. [[CrossRef](#)] [[PubMed](#)]
62. Bruschi, M.L.; Lara, E.H.G.; Martins, C.H.G.; Vinholis, A.H.C.; Casemiro, L.A.; Panzeri, H.; Gremião, M.P.D. Preparation and antimicrobial activity of gelatin microparticles containing propolis against oral pathogens. *Drug Dev. Ind. Pharm.* **2006**, *32*, 229–238. [[CrossRef](#)] [[PubMed](#)]
63. Paula, A.M.B.; Gomes, R.T.; Santiago, W.K.; Dias, R.S.; Cortés, M.E.; Santos, V.R. Susceptibility of oral pathogenic bacteria and fungi to Brazilian green propolis extract. *Pharmacology* **2006**, *3*, 467–473.
64. Popova, M.P.; Chinou, I.B.; Marekov, I.N.; Bankova, V.S. Terpenes with antimicrobial activity from Cretan propolis. *Phytochemistry* **2009**, *70*, 1262–1271. [[CrossRef](#)] [[PubMed](#)]
65. Kim, M.J.; Kim, C.S.; Kim, B.H.; Ro, S.B.; Lim, Y.K.; Park, S.N.; Cho, E.; Ko, J.H.; Kwon, S.S.; Ko, Y.M.; et al. Antimicrobial effect of Korean propolis against the *Mutans Streptococci* isolated from Korean. *J. Microbiol.* **2011**, *49*, 161–164. [[CrossRef](#)] [[PubMed](#)]
66. Liberio, S.A.; Pereira, A.L.; Dutra, R.P.; Reis, A.S.; Araújo, M.J.; Mattar, N.S.; Silva, L.A.; Ribeiro, M.N.S.; Nascimento, F.R.F.; Guerra, R.N.; et al. Antimicrobial activity against oral pathogens and immunomodulatory effects and toxicity of geopropolis produced by the stingless bee *Melipona fasciculata* Smith. *BMC Complement. Altern. Med.* **2011**, *11*, 108. [[CrossRef](#)] [[PubMed](#)]
67. Kousedghi, H.; Ahangari, Z.; Eslami, G. Antibacterial activity of propolis and Ca(OH)₂ against *Lactobacillus*, *Enterococcus faecalis*, *Peptostreptococcus* and *Candida albicans*. *Afr. J. Microbiol. Res.* **2012**, *6*, 3510–3515. [[CrossRef](#)]
68. Bueno-Silva, B.; Alencar, S.M.; Koo, H.; Ikegaki, M.; Silva, G.V.; Napimoga, M.H.; Rosalen, P.L. Anti-inflammatory and antimicrobial evaluation of neovestitol and vestitol isolated from Brazilian red propolis. *J. Agric. Food Chem.* **2013**, *61*, 4546–4550. [[CrossRef](#)]
69. Da Cunha, M.G.; Franchin, M.; de Carvalho Galvão, L.C.; de Ruiz, A.L.; de Carvalho, J.E.; Ikegaki, M.; de Alencar, S.M.; Koo, H.; Rosalen, P.L. Antimicrobial and antiproliferative activities of stingless bee *Melipona scutellaris* geopropolis. *BMC Complement. Altern. Med.* **2013**, *13*, 1–9. [[CrossRef](#)]

70. Dziejdzic, A.; Kubina, R.; Wojtyczka, R.D.; Kabała-Dzik, A.; Tanasiewicz, M.; Morawiec, T. The antibacterial effect of ethanol extract of polish propolis on *mutans Streptococci* and *Lactobacilli* isolated from saliva. *Evid.-Based Complement. Altern. Med.* **2013**, *2013*, 681891. [[CrossRef](#)]
71. Speciale, A.; Costanzo, R.; Puglisi, S.; Musumeci, R.; Catania, M.R.; Caccamo, F.; Iauk, L. Antibacterial activity of propolis and its active principles alone and in combination with macrolides, beta-lactams and fluoroquinolones against microorganisms responsible for respiratory infections. *J. Chemother.* **2013**, *18*, 164–171. [[CrossRef](#)]
72. Barrientos, L.; Herrera, C.L.; Montenegro, G.; Ortega, X.; Veloz, J.; Alvear, M.; Cuevas, A.; Saavedra, N.; Salazar, L.A. Chemical and botanical characterization of Chilean propolis and biological activity on cariogenic bacteria *Streptococcus mutans* and *Streptococcus sobrinus*. *Braz. J. Microbiol.* **2013**, *44*, 577–585. [[CrossRef](#)]
73. Da Silva, J.L.D.C.; Silva, F.F.; de Souza, T.F.M.; Generoso, W.G.; Noronha, V.R.S.; Pereira, E.M.R.; De Luca, M.P.; Abreu, S.; Santos, V. Synergic effect of associated green, red and brown Brazilian propolis extract onto *Streptococcus mutans* and *Streptococcus sanguinis*. *Afr. J. Pharm. Pharmacol.* **2013**, *7*, 2006–2010. [[CrossRef](#)]
74. Hatunoğlu, E.; Oztürk, F.; Bilenler, T.; Aksakallı, S.; Simşek, N. Antibacterial and mechanical properties of propolis added to glass ionomer cement. *Angle Orthod.* **2014**, *84*, 368–373. [[CrossRef](#)] [[PubMed](#)]
75. De Luca, M.P.; Franca, J.R.; Macedo, F.A.; Grenho, L.; Cortes, M.E.; Faraco, A.A.; Moreira, A.N.; Santos, V.R. Propolis varnish: Antimicrobial properties against cariogenic bacteria, cytotoxicity, and sustained-release profile. *Biomed. Res. Int.* **2014**, *2014*, 348647. [[CrossRef](#)] [[PubMed](#)]
76. Ophori, E.A.; Wemabu, E.C. Antimicrobial activity of propolis extract on bacteria isolated from nasopharynx of patients with upper respiratory tract infection admitted to Central Hospital, Benin City, Nigeria. *Afr. J. Microbiol. Res.* **2010**, *4*, 1719–1723. [[CrossRef](#)]
77. Akca, A.E.; Akca, G.; Topçu, F.T.; Macit, E.; Pıkdöken, L.; Özgen, I.Ş. The comparative evaluation of the antimicrobial effect of propolis with chlorhexidine against oral pathogens: An in vitro study. *Biomed. Res. Int.* **2016**, *2016*, 3627463. [[CrossRef](#)]
78. Cardoso, J.G.; Iorio, N.L.; Rodrigues, L.F.; Couri, M.L.; Farah, A.; Maia, L.C.; Antonio, A.G. Influence of a Brazilian wild green propolis on the enamel mineral loss and *Streptococcus mutans*' count in dental biofilm. *Arch. Oral Biol.* **2016**, *65*, 77–81. [[CrossRef](#)]
79. Ertürk, Ö.; Çil, E.; Yoloğlu, N.; Yavuz, C. An In vitro study on antimicrobial and antioxidant activity of propolis from Rize province of Turkey. *Mellifera* **2016**, *16*, 4–18.
80. Oda, H.; Nakagawa, T.; Maruyama, K.; Dono, Y.; Katsuragi, H.; Sato, S. Effect of Brazilian green propolis on oral pathogens and human periodontal fibroblasts. *J. Oral Biosci.* **2016**, *58*, 50–54. [[CrossRef](#)]
81. D'Souza, E.; Mantri, J.; Surti, A. Primary screening of multipotent therapeutic properties exhibited by Indian propolis. *Indian J. Nat. Prod. Res.* **2016**, *7*, 135–140. [[CrossRef](#)]
82. Tiveron, A.P.; Rosalen, P.L.; Franchin, M.; Lacerda, R.C.; Bueno-Silva, B.; Benso, B.; Denny, C.; Ikegaki, M.; De Alencar, S.M. Chemical characterization and antioxidant, antimicrobial, and anti-inflammatory activities of South Brazilian organic propolis. *PLoS ONE* **2016**, *11*, e0165588. [[CrossRef](#)]
83. Abbas, M.J.; Abd Ali, E.H.; Alrawi, R.A. Antibacterial activity of NBF gel against *Streptococcus mutans* isolated from orthodontic patients. *Mustansiria Dent. J.* **2018**, *15*, 58–68.
84. Al-Ani, I.; Zimmermann, S.; Reichling, J.; Wink, M. Antimicrobial activities of European propolis collected from various geographic origins alone and in combination with antibiotics. *Medicines* **2018**, *5*, 2. [[CrossRef](#)]
85. Martins, M.L.; de França Leite, K.L.; Pacheco-Filho, E.F.; de Miranda Pereira, A.F.; Romanos, M.T.V.; Maia, L.C.; Fonseca-Gonçalves, A.; Padilha, W.W.N.; Cavalcanti, Y.W. Efficacy of red propolis hydro-alcoholic extract in controlling *Streptococcus mutans* biofilm build-up and dental enamel demineralization. *Arch. Oral Biol.* **2018**, *93*, 56–65. [[CrossRef](#)] [[PubMed](#)]
86. Roh, J.; Kim, K.R. Antimicrobial activity of Korean propolis extracts on oral pathogenic microorganisms. *J. Dent. Hyg. Sci.* **2018**, *18*, 18–23. [[CrossRef](#)]
87. Santiago, K.B.; Piana, G.M.; Conti, B.J.; Cardoso, E.D.O.; Murbach Teles Andrade, B.F.; Zanutto, M.R.; Rall, V.L.M.; Fernandes, A.; Sforcin, J.M. Microbiological control and antibacterial action of a propolis-containing mouthwash and control of dental plaque in humans. *Nat. Prod. Res.* **2018**, *32*, 1441–1445. [[CrossRef](#)] [[PubMed](#)]
88. Becerra, T.B.; Calla-Poma, R.D.; Requena-Mendizabal, M.F.; Millones-Gómez, P.A. Antibacterial effect of Peruvian propolis collected during different seasons on the growth of *Streptococcus mutans*. *Open Dent. J.* **2019**, *13*, 327–3331. [[CrossRef](#)]
89. Governa, P.; Cusi, M.G.; Borgonetti, V.; Sforcin, J.M.; Terrosi, C.; Bainsi, G.; Miraldi, E.; Biagi, M. Beyond the biological effect of a chemically characterized poplar propolis: Antibacterial and antiviral activity and comparison with flurbiprofen in cytokines release by LPS-stimulated human mononuclear cells. *Biomedicines* **2019**, *7*, 73. [[CrossRef](#)] [[PubMed](#)]
90. Nazeri, R.; Ghaiour, M.; Abbasi, S. Evaluation of antibacterial effect of propolis and its application in mouthwash production. *Front. Dent.* **2019**, *16*, 1–12. [[CrossRef](#)] [[PubMed](#)]
91. Agbor, A.M.; Tsague, R.; Kaptue, B.; Naidoo, S.; Tembe-Fokunang, E.; Fokunang, C.N.; Pilipili, C. Phytochemical characterisation and antibacterial activity of propolis on cariogenic microorganisms. *Eur. J. Med. Plant.* **2020**, *31*, 56–66. [[CrossRef](#)]
92. Rivero-Cruz, J.F.; Granados-Pineda, J.; Pedraza-Chaverri, J.; Pérez-Rojas, J.M.; Kumar-Passari, A.; Diaz-Ruiz, G.; Rivero-Cruz, B.E. Phytochemical constituents, antioxidant, cytotoxic, and antimicrobial activities of the ethanolic extract of Mexican brown propolis. *Antioxidants* **2020**, *9*, 70. [[CrossRef](#)]
93. Alemrajabi, M.S.; Dastorani, M.; Hamidi, H.; Mohammadian, S.; Sadrzadeh-Afshar, M.S. Effects of propolis and persica mouthwashes on three common oral *Streptococci*: A comparative study. *Pharm. Biochem. Res.* **2021**, *7*, 303–316. [[CrossRef](#)]

94. Bapat, S.; Nagarajappa, R.; Ramesh, G.; Bapat, K. Effect of propolis mouth rinse on oral microorganisms- a randomized controlled trial. *Clin. Oral Investig.* **2021**, *25*, 6139–6146. [[CrossRef](#)]
95. Millones Gómez, P.A.; Tay Chu Jon, L.Y.; Maurtua Torres, D.J.; Bacilio Amaranto, R.E.; Collantes Díaz, I.E.; Minchón Medina, C.A.; Calla Choque, J.S. Antibacterial, antibiofilm, and cytotoxic activities and chemical compositions of Peruvian propolis in an in vitro oral biofilm. *F1000Research* **2021**, *10*, 1093. [[CrossRef](#)]
96. Hajiahmadi, M.; Faghri, J.; Salehi, Z.; Heidari, F. Comparative Evaluation of Antibacterial Effect of Propolis and Aloe Vera, Xylitol, and Cpp-Acp Gels on *Streptococcus mutans* and *Lactobacillus* in vitro. *Int J. Dent.* **2021**, *2021*, 5842600. [[CrossRef](#)] [[PubMed](#)]
97. Ismail, T.N.N.T.; Wee, N.S.C.; Shafii, N. Antimicrobial activity of propolis from *Trigona thoracica* towards cariogenic bacteria. *Malays. Appl. Biol.* **2021**, *50*, 65–71. [[CrossRef](#)]
98. Navarro-Pérez, M.L.; Vadillo-Rodríguez, V.; Fernández-Babiano, I.; Pérez-Giraldo, C.; Fernández-Calderón, M.C. Antimicrobial activity of a novel Spanish propolis against planktonic and sessile oral *Streptococcus* spp. *Sci. Rep.* **2021**, *11*, 23860. [[CrossRef](#)]
99. Günçe, O.Z.A.N.; Meltem, M.E.R.T.; Vatanserver, C. Antimicrobial effect of propolis drops on oral pathogens in vitro. *Selcuk Dent. J.* **2021**, *8*, 673–678. [[CrossRef](#)]
100. Onur, E.; Gökmen, G.G.; Nalbantsoy, A.; Kışla, D. Investigation of the supportive therapy potential of propolis extract and *Lactobacillus acidophilus* LA-5 milk combination against breast cancer in mice. *Cytokine* **2022**, *149*, 155743. [[CrossRef](#)]
101. De Carvahlo Duailibe, S.A.; Gonçalves, A.G.; Ahid, F.J.M. Effect of a propolis extract on *Streptococcus mutans* counts in vivo. *J. Appl. Oral Sci.* **2007**, *15*, 420–423. [[CrossRef](#)]
102. Machorowska-Pieniążek, A.; Morawiec, T.; Mertas, A.; Tanasiewicz, M.; Dzedzic, A.; Król, W. Influence of propolis on hygiene, gingival condition, and oral microflora in patients with cleft lip and palate treated with fixed orthodontic appliances. *Evid.-Based Complement. Altern. Med.* **2013**, *2013*, 183915. [[CrossRef](#)] [[PubMed](#)]
103. El-sayed, S.; El-Bayoumy, S.; Mostafa, M.; EL-Malt, M. Evaluation of the antimicrobial effect of propolis extract on oral microflora. *Al-Azhar Dent. J. Girls* **2016**, *3*, 135–140. [[CrossRef](#)]
104. El-Allaky, H.S.; Wahba, N.A.; Talaat, D.M.; Zakaria, A.S. Evaluation of antimicrobial effect of two propolis formulae on *Streptococcus mutans* and *Candida albicans*: A randomized clinical trial. *Alex. Dent. J.* **2020**, *45*, 99–103. [[CrossRef](#)]
105. Alkhaled, A.; Alsabek, L.; Al-assaf, M.; Badr, F. Effect of chlorhexidine, honey and propolis on *Streptococcus mutans* counts: In vitro study. *Dentistry 3000* **2021**, *9*, 107–117. [[CrossRef](#)]
106. Mohsin, S.; Manohar, B.; Rajesh, S.; Asif, Y. The effects of a dentifrice containing propolis on *Mutans Streptococci*: A clinico-microbiological study. *Ethiop. J. Health Sci.* **2015**, *25*, 9–16. [[CrossRef](#)]
107. Lotif, M.; Valadas, L.; Fechine, F.V.; Fonseca, S.; Bandeira, M.; Dantas, T.; Rodrigues Neto, E.M.; Squassi, A.; Fonteles, M.M.F. A double-blind randomized clinical trial of Brazilian red propolis dentifrice efficacy in orthodontic patients. *J. Oral Sci.* **2022**, *64*, 28–32. [[CrossRef](#)] [[PubMed](#)]
108. El Naggar, R.A.; Ibrahim, S.H.; Mosallam, R.S.; Khairy, M.A. Effect of propolis and pomegranate extract mouthwashes on taste alteration, salivary pH and antibacterial activity in high caries risk patients: A randomized control trial. *Indian J. Public Health Res. Dev.* **2021**, *12*, 463–470. [[CrossRef](#)]
109. Nakao, R.; Ueno, T. Effects of oral moisturizing gel containing propolis following head and neck radiotherapy: Randomized controlled pilot trial. *BDJ Open* **2021**, *7*, 1–7. [[CrossRef](#)]
110. Siqueira, É.C.; Campos, F.M.T.; Mendes, J.C.; De Lima, L.N.; Araújo, R.S.; Gomes, N.K.S.; da Silva Lima, L.R.; Nogueira, R.F.; Rocha, M.C.; Barros, R.J.V. Evaluation of the effects of propolis and xylitol chewable tablets on the salivary concentrations of oral micro-organisms in orthodontic patients: A pilot study. *J. Young Pharm.* **2021**, *13*, 68. [[CrossRef](#)]
111. Wiatrak, K.; Morawiec, T.; Rój, R.; Kownacki, P.; Nitecka-Buchta, A.; Niedzielski, D.; Wychowański, P.; Machorowska-Pieniążek, A.; Cholewka, A.; Baldi, D.; et al. Evaluation of effectiveness of a toothpaste containing tea tree oil and ethanolic extract of propolis on the improvement of oral health in patients using removable partial dentures. *Molecules* **2021**, *26*, 4071. [[CrossRef](#)]
112. Seth, T.A.; Kale, T.A.; Lendhey, S.S.; Bhalerao, P.V. Comparative evaluation of subgingival irrigation with propolis extract versus chlorhexidine as an adjunct to scaling and root planing for the treatment of chronic periodontitis: A randomized controlled trial. *J. Indian Soc. Periodontol.* **2022**, *26*, 151–156. [[CrossRef](#)]
113. Ratajczak, M.; Kaminska, D.; Matuszewska, E.; Hołderna-Kedzia, E.; Rogacki, J.; Matysiak, J. Promising antimicrobial properties of bioactive compounds from different honeybee products. *Molecules* **2021**, *26*, 4007. [[CrossRef](#)]
114. Luo, X.; Dong, Y.; Gu, C.; Xueli, Z.; Haile, M. Processing technologies for bee products: An overview of recent developments and perspectives. *Front. Nutr.* **2021**, *8*, 834. [[CrossRef](#)]